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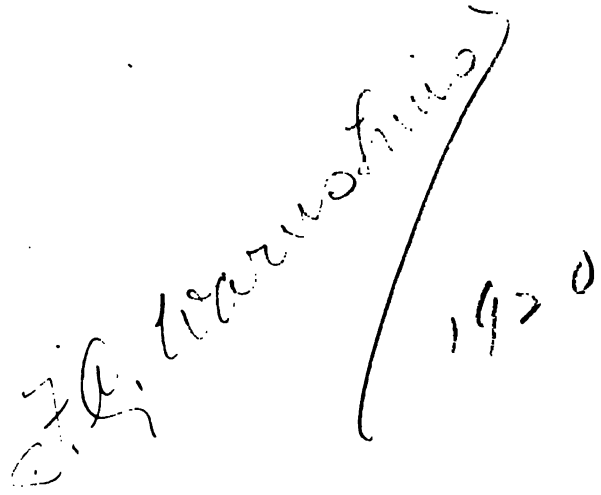
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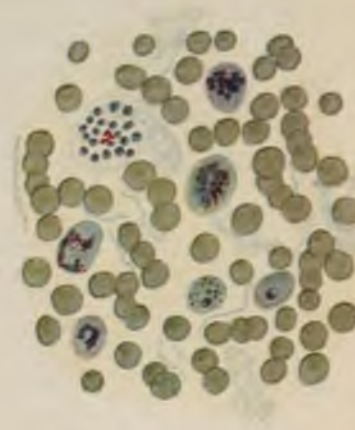
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PLATE I.—1, Tænia solium; 2, Malaria parasite (tertian); 3, Treponema pallidum; 4, Trypanosoma gambiense.

HUMAN PARASITOLOGY

WITH NOTES ON

BACTERIOLOGY, MYCOLOGY, LABORATORY DIAGNOSIS, HEMATOLOGY AND SEROLOGY

By

DAMASO RIVAS

B. S. Biol., M. S., M. D., Ph. D.

Assistant Professor of Parasitology; Assistant Director of the Course in Tropical Medicine and of the Laboratory of Comparative Pathology and Tropical Medicine in the University of Pennsylvania; Pathologist to the Department of Health of Pennsylvania; Serologist to Friends Hospital, Frankford; Assistant Pathologist to the Philadelphia General Hospital; Ex-Research Fellow in Biology and Ex-Scott Fellow in Hygiene, University of Pennsylvania; Formerly Assistant to the Koch Institute, Berlin, and Co-worker in the Pasteur Institute, Lille; Member of the Malaria and Tropical Diseases Commission for the Sanitation of Brioni, Istrie and East Shores of the Adriatic, 1900–1902

ILLUSTRATED

PHILADELPHIA AND LONDON

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1920

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To

ALLEN J. SMITH

M. D.; Sc. D.; LL. D.

Professor of Pathology and Comparative Pathology

In the Medical School of the

University of Pennsylvania

This Volume

Is Dedicated as a Token of Respect and Gratitude

By His Pupil, Assistant and Friend

THE AUTHOR

87392

PREFACE

A half century ago medicine was more an art than a science. The doors of American medical colleges stood wide open to welcome all who came as students, and if they showed a desire to learn, possessed enough elementary education to enable them to read their text-books and write their examination papers, no questions were asked as to their acquaintance with the physical and biologic sciences.

A few of the professors were men learned in science or letters, but the greater number knew the subjects they taught, understood "practice" or the art of their profession, and little else, looking with suspicion or distrust upon their colleagues who "wasted their time" upon the pursuit of the collateral sciences.

There was no science of parasitology. Parasites were zoölogic curiosities that occasionally intruded into the sphere of medical activity. Most of the text-books informed the reader that the Tænia solium was the common tapeworm of the United States, not because the writer knew the worm or had identified it, but because the European text-books which he used in compiling his own, so informed him. Thus he misinformed his readers. If the student learned how to kill a tapeworm, how to cause the expulsion of round worms (Ascaris lumbricoides) and seat-worms (Oxyuris vermicularis) he could well rest satisfied. Additional information might be needed by those who engaged in missionary work in the tropics, but that was a matter that concerned them alone.

Now all has changed. The necessities of commerce have led to such extensive geographic explorations that the entire surface of the earth has been explored and charted. Ethnologic investigators have uncovered the location, life and habits of many formerly unknown peoples. The demand for ivory, furs, rubber, and other commodities of wild, and especially tropical countries, has been followed by the dissemination of white men throughout the world. Improvement in transportation, increase in commerce, the exploitation of the savage by the civilized peoples, the exigencies of war, in tropical wildernesses, carried on for the purpose of facilitating the exchange of commodities, have all greatly increased the number of medical men whose time is largely spent amid new and unusual surroundings in which they find new and strange diseases, some of which they and their patients bring back to their European or American homes.

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The general rapid advance of scientific knowledge, especially the progress of physics, chemistry and biology, inevitably reacted upon medicine, stimulating the scientific spirit, demanding research upon its obscure problems, and requiring a new type of student whose preparation for medicine must include at least a elementary knowledge of the collateral and fundamental sciences.

To gain admission to the medical college it became necessary to know physics, biology and chemistry. In the college the instruction ceased to be didactic and clinical. It became practical as well; the laboratory and the microscope became essential to it.

The abandonment of the doctrine of spontaneous generation, the evolution of the germ theory of disease, the discovery of the specific bacteria of many of the infectious diseases, the discovery of the malarial plasmodium, of the cause of kala-azar and of sleeping sickness, changed the general attitude of the medical profession. It was recognized that many well known diseases were caused by microparasites, others might be. Parasitologic investigations were worth while; students ought to be instructed how to conduct them. Thus parasitology, a subject essentially biologic gradually became medical, and took its place in the medical curriculum as too important to be longer neglected. The subject has in a few years grown to great proportions and to great importance. It is now considered that at least a third of the human diseases are caused by parasites.

The author has for twenty years interested himself in parasitology and has had the good fortune to have studied in public health laboratories at home and abroad and to have served on sanitary commissions. After years of teaching he now endeavors to bring together the facts of parasitology in a form suitable to the needs of the student and physician. The following pages reflect his personal experiences and present the facts of the subject in a form sufficiently brief to make it a text-book—the modern tendency is to be encyclopedic—and sufficiently full not to omit any important fact or method.

The ever changing nomenclature of parasitology is a continued source of embarrassment to students. One scarcely knows that a worm is called Ankylostoma before he finds that the name is changed to Agchylostoma, scarcely learns to recognize it in print before he finds it spelled Ancylostoma, and there are chances that before long he may meet with it in the form Agkylostoma. An organism well known as Endameba is suddenly called Loeshia, and Trypanosoma ugandense, about the time he gets well acquainted with it, suddenly becomes Castellanella castellanii.

The author has kept himself informed upon these changes of nomenclature, but confesses that he is not in favor of them except when definite improvement can be shown. He therefore has made conscientious

efforts to follow the rules of the International Committee upon Zoölogical Nomenclature, and has avoided the introduction into his book of certain new generic and other names that have not yet been generally adopted.

To certain of his friends and colleagues the author is deeply indebted for assisting him in a variety of ways, and takes this opportunity to render them his sincere thanks.

D. RIVAS.

UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,
May, 1920

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HUMAN PARASITOLOGY

PART I

INTRODUCTORY

CHAPTER I

HISTORY OF PARASITOLOGY

In primitive times many curious beliefs existed as to the origin of disease. Thus diseases were attributed to supernatural causes, such as evil, offended spirits, Divine punishment, astronomic phenomena, etc., and many of these beliefs still prevail in certain countries. Although primitive people did not understand the cause of disease, they nevertheless possessed a general knowledge of medicinal plants, using them in the treatment of their ailments, as is shown by the existence of a system of primitive medicine among the Chinese, Japanese, Aryan, Aztec, Inca, and other races.

The Aryan race possesses the *Ayurveda*, a medical book that is believed to have originated directly with Brahma; it was later corrected by Charaka, whose name it bears. This race also possesses another book, by Susruta, in which fevers are attributed to the bites of mosquitos.

There are also numerous evidences that the Indian doctors possessed a fair knowledge of diabetes mellitus, dysentery, syphilis, phthisis, and diseases due to worms, but the date of these books is not known.

It is probable that the Egyptians had some knowledge of the presence of hookworm in the intestine. The Ebers papyrus, which dates back to about 1550 B.C., besides containing information concerning remedies for diseases of the stomach, abdomen and urinary bladder, also gives an account of a disease called *'AAA'* and *'UHA.'*, caused by Heltu, probably ankylostoma, although it may possibly refer to ascaris, tape-worm, or oxyuris, which, being passed by the rectum, would easily be recognized.

In the Book of Numbers a disease is described caused by fiery serpents, which probably refers to guinea-worm (*Dracunculus* or *Filaria medinensis*), and it appears that Moses taught the Jews how to extract the worm by means of winding it around a stick.

The classification of diseases into acute (plague) and chronic (leprosy) disorders, which was made during the Mosaic period, is very imperfect, but the careful hygienic measures of the time, and the division of animals into clean and unclean, so that the people could avoid those that were infested, show clearly that the Jews had some knowledge of certain parasitic diseases, and were also familiar with the mode of transmission by eating flesh infested with those parasites that are easily seen, such as beef and pork tape-worms.

Hippocrates (460 B.C.) distinguished intermittent from continuous fever, differentiated the three types of malarial fever (tertian, quartan, and subtertian), noted their occurrence during summer and autumn and the prevalence of the disease in swampy localities and after rain.

Agatharchides (170 B.C.) described dracunculus; Celsus (29 B.C.) divided malaria into benign and malignant forms; Aretæus (30–90 A.D.) studied dysentery; and Galen (131–210 A.D.) gave a careful description of tertian and quartan malarial fever.

Paulus (1700) gives an interesting summary of medicine from the time of Galen to the end of the seventeenth century, and in his fourth book refers to the flat and round worms and to ascaris and dracunculus.

Modern medicine may be said to have originated with the domination of the Arabs in Spain and at the time of the Crusades. With the importation into Europe of diseases peculiar to the Orient, such as leprosy, plague, typhus fever, and probably syphilis, the particular attention of physicians was aroused. Although these diseases may have existed in western Europe since the Roman domination, they were apparently not so prevalent as to attract the attention of the medical men of earlier times. Strict quarantine regulations were enforced against leprosy, and a systematic study of this and of other diseases was begun.

The introduction into Europe of Jesuit's bark, or quinin, in 1670, and the recognition of the specific value of the drug in the treatment of malaria, served to differentiate malaria from other diseases with which it had been confounded. The foundation of modern parasitology was laid, however, when it was recognized that parasites were the common causes of disease.

Though round and tape-worms were known to the ancients, it was not until 1379 that the first trematode, *Fasciola hepatica*, was discovered by de Brie in the liver of a sheep. The knowledge of this parasite was extended by Gabucinus (1547), Leeüwenhöek (1675), Swammerdam, Rosenhof (1758), Müller (1777), and Zeder. In 1800 Zeder gave the name "sucking-worm" to these animals, and Rudolphi, in 1803, suggested the name Trematodes ("pierced with holes").

The knowledge of parasites has been greatly advanced since the

discovery of the hookworm (Ankylostoma duodenale) by Dubini in 1838; of Schistosoma by Bilharz in 1851; of *Opisthorchis noverca* by Cobbold in 1859; of Filaria by Demarquay in 1863; and of *Paragonimus westermanii* by Kerbert in 1878.

Of great importance have been the classic studies of Leuckart and van Beneden on Trematodes; of Thomas, who, in 1883, worked out the life history of *Fasciola hepatica*, and of Küchenmeister, who, in 1851, proved by feeding experiments that the cysticerci of Redi and Zeder, considered by them as a separate species of animal, were only the larval stage of tape-worms, two hosts being required in the life history of these parasites.

Mention should also be made of the work of Sonsino, Perroncito, Braun, and Looss, who demonstrated the penetration of the larva of the hookworm through the skin, and of Stiles, who, in 1902, differentiated the two species of the parasite, *Ankylostoma duodenale* and *Necator americanus*. Stiles's observations have been corroborated by Looss and others. More recently important contributions on parasitology have been made by Railliet, Blanchard, and Brumpt in Paris; Linstow, Sambon, and Leiper in London; Ashburn, Craig, Musgrave, and others in the Philippine Islands; Miura and Katsurada in Japan, and Castellani and others in India.

Demarquay, in 1863, in Paris, discovered a *Microfilaria* in the liquid from a hydrocele; Wucherer, in 1866, and Lewis, in 1868, found it in the urine. Lewis also found it in the blood and Bancroft in 1876–77, discovered the adult filaria in an abscess. Manson, however, stands out preëminently in that he showed, in 1881, the relation between filariasis and elephantiasis. In the following year he demonstrated the periodicity of the appearance of the embryos in the peripheral blood; and as early as 1877 he observed the development of microfilaria in the mosquito, and suggested the possible transmission of the parasite by this insect, thus laying the foundation for the study of the development of the malarial parasite in the mosquito.

Protozoan organisms were recognized by Leeüwenhöek in 1675, and the first life history was worked out in Vorticella by Tembley in 1744.

The first parasitic protozoan of man to be discovered was *Balantidium coli*, which was found by Malmsten in 1856. *Lamblia intestinalis* was discovered by Lambl in 1859; and Davaine discovered *Trichomonas hominis* in 1864. These three parasites inhabit the large intestine, and are regarded as the cause of certain diarrheas in man.

As early as 1860 Lambl described the presence of motile amebæ in the stools of a case of diarrhea, and in 1870 Lewis found the same organism in a case of cholera. In 1875 Lösch found the parasite in a

case of chronic diarrhea, and named it *Amœba coli*. Sonsino, Koch, and Kartulis corroborated Lösch's observation, and pointed out the probable relation of the parasite to dysentery. Other observers, however, such as Grassi, Celli, etc., found similar organisms in healthy persons. Kruse and Pasquale first suggested the possible existence of two species of ameba—one pathogenic and the other innocuous. In 1905 Schaudinn confirmed the opinion that there were two species, one being non-pathogenic; to this he gave the name of *Entamœba coli*, and to the pathogenic variety he gave the name of *E. histolytica*. The latter he regarded as the cause of tropical dysentery and of amebic abscess of the liver.

The discovery, by Laveran, in 1880, of the malarial parasite, and that of Golgi, Marchiafava, Celli, Bignami, and others, who differentiated three varieties of the parasite (tertian, quartan, and quotidian), demonstrated the asexual cycle of the parasite in the blood of man, and established its relation to the clinical manifestations of the disease

Adopting the suggestion of Manson that the malarial parasite developed like microfilaria in the body of the mosquito, Ross succeeded in demonstrating the development of a bird parasite (Proteosoma) in Culex, and Grassi showed the development of the tertian malarial parasite of man in *Anopheles*. These observations were quickly verified by Marchiafava, Celli, Bignami, Dionisi, and others, but the name of Schaudinn stands out prominently in this connection, for in his classic work on the Coccidia he had previously demonstrated a similar life history. Thus the theory of the transmission of malaria by mosquitos was proved.

Among the flagellates, Ford, in 1901, discovered a trypanosoma in the human blood to which Dutton, in the following year, confirming Ford's observation gave the name of T. gambiensis; he noted its occurrence in sleeping sickness; Castellani, in 1902, found the parasite in the cerebrospinal fluid. These observations and those of Bruce, Nabarro, and others finally established the fact that *Trypanosoma gambiensi* was the cause of the "sleeping sickness" in Africa, and that the parasite was transmitted to man by the "tsetse fly," *Glossina palpalis*. In 1900 Leishman found peculiar intracellular bodies (*Leishmania donovani*), in cases of Indian "kala-azar;" these were later shown to be the cause of the disease. In 1909 Chagas found that the *Trypanosoma cruzi* was the cause of American trypanosomiasis.

All these discoveries, however, are based on the work of Evans, who, in 1880, found the *Trypanosoma evansi* to be the cause of "*surra*," thus demonstrating the fact that trypanosomes may be pathogenic, although these organisms had previously been regarded as harmless. Other important discoveries were that of Bruce, who found *T. brucei*

to be the cause of "Nagana," and that of Rouget, who discovered that *T. equiperdum* was the cause of "dourine."

As regards the spirochetes, Obermeier in 1873 discovered the spirochete of relapsing fever. This was believed to be a solitary variety, but as the result of the work of Nabarro, Todd, Ross, Dutton, Novy, and others, four distinct kinds of spirochetes are now recognized, causing respectively the European, African, Indian, and American forms of relapsing fever. Schaudinn, in 1905, announced the discovery of *Treponema pallidum* as the cause of syphilis; and Castellani found *T. pertenue* to be the cause of "yaws."

Reference should also be made to the discovery by Babes, in 1888, of a small protozoon, *Babesia bigeminum*, commonly known as Piroplasma, in the blood of cattle; this is now recognized as being the cause of "Texas fever." Attention should also be called to the work of Smith and Kilbourne, who showed that the transmission of the parasite is accomplished by a tick. Inasmuch as the "spotted fever" of the Rocky Mountains is also transmitted by the tick, it was suspected that a *Babesia* might also be the cause of that disease, but nothing definite has been determined. Ricketts described a bacillus-like organism found in this disease, and others have observed certain intercellular bodies.

In recent years a great deal of attention has been paid to the study of certain protozoa-like bodies, to which, because of their usual occurrence inside of the cell, the name "cell inclusions" or "inclusion bodies" is commonly given. These bodies were first described by Negri, who, in 1903, discovered them in cases of hydrophobia. Negri bodies are now regarded as protozoa, and as being the cause of hydrophobia. Somewhat similar bodies have been found in scarlatina, variola, etc., but their precise nature has not been definitely determined.

Mention must also be made in this connection of certain forms of life that are so minute as to be invisible under the microscope, and that are capable of passing through the pores of the finest porcelain filter. To these bodies the collective name of "filterable virus" has been given. For many years the existence of such ultramicroscopic forms of life had been suspected, but it was not until 1898 that Loeffler and Frosch showed that the virus of foot-and-mouth disease could pass through the finest porcelain filter. In 1899–1900 Frosch and Rivas made similar observations with chicken pest, and Beijernick also observed similar results with the mosaic disease of the tobacco plant.

Some conception as to the amount of work done along this line is shown by the number of diseases—thirty in all—now attributed to these ultramicroscopic organisms. Among the diseases produced by filtrable virus some are peculiar to man, *e.g.*, yellow fever, typhus fever,

poliomyelitis, molluscum contagiosum, etc.—whereas others occur in man and the lower animals, as, for example, foot-and-mouth disease, hydrophobia, and the like.

Bacteriology undoubtedly has been an important contributing factor in the development of parasitology, because it has at least served to differentiate bacterial from protozoan diseases. Nevertheless all knowledge concerning the etiology of disease is based on the evolution of the microscope. This valuable instrument has, as it were, developed a "sixth sense" in man, and placed the science of bacteriology and of protozoölogy upon a firm basis.

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CHAPTER II

GENERAL REMARKS ON PARASITOLOGY AND PARASITES

Parasitology and its Object.—Mode of Investigation.—Nomenclature.—Definition of a Parasite: Symbiosis; Commensalism; Parasitism.—Habitat.—Varieties of Parasites and Degree of Parasitism.—Life History.—Teleology of Parasites.—Mode of Dissemination and Transmission.—Vitality of Parasites: Intensity of Infection.—Effect of Parasitism upon the Parasite.—Effect of Parasitism upon the Host.—Pathogenesis in Parasitic Infestation.—Defense of the Organism.—Ultimate Fate of Parasites.—Pseudo-parasites.

Parasitology and its Object.—Parasitology is the science that deals with the life history of plants and animals living at some stage of their life cycle wholly or in part in or upon other plants or animals. The name parasite is given to such organisms since they are dependent for their subsistence upon a host, in whom they produce more or less grave disturbances, *i.e.*, morbid changes.

Parasitology deals primarily with the morphology of the parasite. It treats of the biology and life history from the development of the egg or germ to the adult stage; the physicochemical agencies favorable or detrimental to the development and life of the parasitic organism; the mode of infestation or the means by which it gains entrance to the body of the host; and the changes that take place in the host as the result of the mechanical, toxic, or infectious activities of the organism.

Parasitology is a valuable adjunct to pathology, determining, as it does, the biologic causes of disease, the localization of the parasite in the body, and the agencies concerned in the production of morbid changes. It furnishes a plausible explanation for the symptoms of the disease. Nevertheless a knowledge of the life history and of the effect of environmental conditions is of untold value in hygienic prophylaxis and in general sanitation.

Mode of Investigation.—In order to prove the parasitic nature of a suspected organism, it is necessary that it be introduced into a favorable host. Progress in the study of human parasitology has been slow, owing to the fact that experimentation on human beings is interdicted and generally condemned. Some parasitic diseases are common both to man and to the lower animals, as for instance, trichiniasis, etc. Under such circumstances, by experimenting upon susceptible animals, many doubtful points in human parasitology can be satisfactorily cleared up and the means for curing or preventing disease discovered. The advantages thus gained, however, may be offset

by the fact that it may not be possible to control the spread of a disease among animals, even after its cause and prophylaxis are thoroughly understood. In order to understand the nature of epidemics and to prevent the transmission of many diseases, it is essential, therefore, that hygienists and physicians have some knowledge of the parasitic diseases of animals.

Nomenclature.—As the result of international agreement, naturalists now follow certain fixed rules as regards nomenclature. Every living organism has been given two names: The first or generic name indicates the genus, and the second, or specific name, indicates the species, and are derived from the Latin or Greek; *e.g.*, *Fasciola hepatica*. The subspecies usually have three names, as, for example, *Tænia echinococcus multilocularis*.

The name of the species frequently, but not necessarily, indicates some distinctive characteristic, as that of shape, habitat, color, etc., or it may take the name of the author who first described it. The name of a family is usually formed by adding the suffix *idæ*, and that of a sub-family, *inæ*, to the radical of the oldest genus in the family. The common house-fly, *Musca domestica*, may be taken as an example: thus the species is *domestica*, the genus *Musca*, the sub-family *Muscinæ*, the family, *Muscidæ;* the suborder, *Brachycera;* the order, *Diptera*, and the class *Insecta*; which belongs to the phylum *Arthropoda*.

In describing the species, the name of the author (often abbreviated) and the date on which the description first appeared are always given; for instance, *Fasciola hepatica* was named by Linnæus in 1758, and should be written *Fasciola hepatica* Linn., 1758. This same author in 1758 gave the name *Culex bifurcatus* to a certain variety of mosquito. Meigen, in 1818, observing that there were structural differences of considerable importance between certain of the species in the genus Culex, provided for them by constructing a new genus, namely, Anopheles. Where such conditions exist the specific name remains the same, but the name of the author is added in parenthesis, indicating that the genus of the species has been changed; as, for instance, *Anopheles bifurcatus* (Linn., 1758).

Definition of a Parasite.—When two organisms habitually live together, the relationship is designated biologically as *symbiosis*, each organism being called a *symbiont*. If the relationship is one of mutual advantage, that is, if each supplies the other with substances that are useful or essential to its existence, as is the case, for example, between *Bacillus radicicola* and leguminous plants, this constitutes what is known as *mutualism*.

If one symbiont lives on the other (the host) without either benefiting or injuring it, the smaller symbiont is called an *inquiline* or a *commensal*, and such symbiotic relationship is known as *commensalism*.

Thus the small pea-crab (Pinnotheres) is a commensal living within the shell of an oyster, but feeding independently of it. Other examples are found among certain trematodes that have an ectoparasitic existence on the gills and about the mouths of fishes.

When the smaller organism lives either temporarily or permanently in or upon and at the expense of the other, deriving its food from it but giving nothing in return, it is called a *parasite;* and the symbiotic relationship that exists between the two is known as *parasitism*. The term parasitism, therefore, implies the subsistence of one organism, —the smaller (the parasite)—in or upon and at the expense of the other—the larger (the host)—to the detriment of the latter.

Habitat.—Parasites have been found in every portion of the human body, but certain structures seem to be especially well adapted to their life requirements. This is dependent in large measure upon some physicochemical property inherent in the part affected. If the parasite fails to reach the suitable organ or tissue, or in the case of its experimental transplantation to an organ or a tissue that is not adapted to its requirements it generally dies.

Ascaris and "hookworm" inhabit the small intestine; Trichocephalus, the cecum; *Fasciola hepatica*, the liver; *Paragonimus westermanii*, the lungs, and *Filaria bancrofti*, the lymphatics. These parasites may, however, be found at some distance from their usual or normal habitat; thus Ascaris has been found in the stomach; *Fasciola hepatica*, in the lung, and Paragonimus, in the liver. The term "erratic parasite" is applied to a parasite that is found in an unusual situation, an irregularity not uncommonly associated with exceptionally marked infestment, concomitant disease of the host, or other complications that, by changing the chemistry of a part, make it a suitable environment for the parasite. This may also explain the occasional occurrence, in man, of certain parasites peculiar to animals, a condition that has been termed "occasional parasitism" by Davaine.

Variety of Parasites and Degree of Parasitism.—The parasites of man are divided into two main groups, namely, *ectoparasites* and *endoparasites*. The former term is applied to those parasites that live temporarily or permanently upon the outside of the body—on the skin or its appendages or on the mucous membranes of the normal external cavities (mouth, ear, nose, etc.). *Sarcoptes scabiei* and many fungi are ectoparasites. The second term is applied to those parasites that live within the host, as, for example, *Plasmodium malariæ* and *Fasciola hepatica*. To some organisms the parasitic life is indispensable to their existence, and to them the name of *obligatory parasites* has been given; among these are the Plasmodium, Trypanosoma, Trichinella, etc. Organisms that do not require a parasitic existence are termed

optional or *facultative parasites.* As examples of the latter the diptera larvæ and *Strongyloides intestinalis* may be cited.

When the parasite visits the host only at intervals, it is called an *occasional, temporary,* or *periodic parasite,* as *e.g.,* fleas, ticks, leeches, mosquitos, and bedbugs. When the parasite remains in the host from early life until maturity, it is known as a *permanent parasite;* the tapeworms, Trichinella and Plasmodium, are examples of permanent parasites. It will be seen that all permanent parasites are obligatory parasites, but that all obligatory parasites are not necessarily permanent parasites. Finally, the name *zoö-parasite* is applied to animal parasites, and the name *phyto-parasite* is given to vegetable organisms.

Life History.—The life of the parasites in general differs in no essential way from that of free living forms, except that they commonly require a special environment or host for their development. There are two methods of development, the direct and the indirect. In the former method no intermediate host is required, whereas in the latter a second host in necessary to complete the life history. As a rule, the more dependent the parasite is upon its host, the more likely is its life cycle to be complicated. Thus, among unicellular parasites, the life cycle of *Endameba histolytica* (the parasite of tropical dysentery), for instance, does not differ materially from the life cycle of *E. coli* (a saprozoön of the large intestine), or from any of the free-living forms of ameba. *Endameba histolytica* may be taken as illustrative in this case, since it represents a low degree of parasitic life. Like *E. coli, E. histolytica* feeds chiefly on decayed matter and inhabits the large intestine, although in marked infestment it may invade the liver. The entire existence of this parasite is extracellular.

A higher form of parasitic life is represented by the Coccidia, a species of which inhabits the bile-ducts of rabbits. The parasite lives an intracellular existence in the epithelial cells of the bile-passages, but is not known to exist in the blood. The life cycle of this parasite is more complicated, and although it requires only one host, the asexual reproduction, or *schizogony,* is sharply differentiated from the sexual, or *sporogony.*

The highest type of parasitic evolution among protozoa may be said to be represented by the hematozoa of malaria, which have an asexual intracellular existence in the erythrocytes, and an extracellular sexual development in the mosquito.

What has been said regarding parasitic protozoa applies also to parasitic metazoa. Thus the life cycle of *Strongyloides intestinalis,* which is a facultative parasite, does not differ essentially from that of some of the free-living nematodes. As the parasitic habit becomes better developed, as in Ascaris, Ankylostoma, Trichinella, etc., the life history becomes more complex; it is more complex in Filaria, which

requires two hosts for its complete development. Cestodes and trematodes also have complicated life cycles. In the life history of obligate parasites, such as *Fasciola hepatica*, for instance, there are two free living larval stages and two parasitic stages in two different hosts.

From what has been said it will be seen that in order to complete its life history a parasite may need to establish a residence in one or two hosts. This peculiarity divides these organisms into two main groups—the *monoxenous*, requiring one host, and the *heteroxenous*, requiring two hosts. Amebæ, coccidia, ankylostoma, fleas, lice, etc., are examples of monoxenous parasites. Such parasites may either pass their entire existence in or on the host (*e.g.*, lice), or a portion of their development may take place apart from the host, as is the case in amebæ, coccidia, ankylostoma, fleas, etc. During this outside existence the parasite undergoes certain changes preparatory to and essential for its successful entrance and retention in another host. Thus Amebæ and coccidia undergo encystment; ascaris develops into a larva, and in ankylostoma, the larva, after escaping from the egg becomes encysted in one of its moults.

The malarial parasite *Fasciola hepatica*, *Filaria bancrofti*, and trichinella are examples of heteroxenous parasites. The host in which the parasite undergoes sexual reproduction is called the *primary* or *definitive* host, whereas that in which it undergoes asexual reproduction, or merely a stage of development, is called the *secondary* or *intermediate* host. Thus the mosquito is the primary and man the secondary host of the plasmodium of malaria; a man or a sheep may be the primary host and a snail the secondary host of *Fasciola hepatica*. In certain cases, such as that of *Trypanosoma gambiensis* (the cause of sleeping sickness), which requires a second host for its transmission, the tsetse fly is perhaps the primary host; the life history of this parasite and its sexual reproduction are not as yet completely understood.

Teleology of Parasites.—It is impossible here to do more than theorize upon the way in which the parasitic mode of life has been adaptated. The habits of the parasites and their behavior and varied adaptations suggest their descent from related independent forms of life. Thus, probably in the same manner in which pathogenic bacteria are believed to have originated from saprophytes—*i.e.*, through changes and adaptation to new environments—so among the zoöparasites similar changes and adaptations are seen that show a gradual transformation from the free living and saprozoic life to the typical parasitic existence.

Among the rhizopods, *Endamœba coli*, for instance, probably originated from a free-living ameba, which, by being repeatedly swallowed, acquired a parasitic habit *E. coli;* and this, under peculiar circumstances and with a more markedly accentuated parasitic existence, may have

given rise to *Endamœba histolytica*, which is an obligate parasite and the cause of tropical dysentery in man. *E. histolytica*, though manifesting a tendency to migrate to the liver, does not live in the blood. Recent studies have shown the common relationship that exists between rhizopods and sporozoa, and it is not improbable that, in the course of parasitic evolution, some such endameba as *E. histolytica* became a coccidium and later a parasite of the blood, as a lower form of hematozoön from which finally the hematozoön of malaria may have originated.

Among the flagellates the same gradation perhaps exists. It is possible that the free living forms of spirochetes found in water gave rise to the parasitic ones found in the lower animals, and these to the occasional parasites, as in Vincent's angina, found in the mouth of man. From these pathogenic species may have originated, such as *Spirochæta recurrentis*, the cause of relapsing fever; *Treponema pertenue*, the cause of yaws; and *T. pallidum*, the cause of syphilis. It is of interest to note that morphologically the two organisms *T. pertenue* and *T. pallidum* are almost identical; and the diseases caused by them, yaws and syphilis respectively, have many things in common, so that in a broad sense it might be conjectured that the syphilitic treponema represents a malignant variety of the treponema of yaws.

Similar examples are found among trypanosomes; from the saprozoic type of crithidia and herpetomona, found in the digestive tract of insects and invertebrates, one may imagine a transition to the parasitic, but apparently nonpathogenic, species, as *Trypanosoma rotatorium* of the frog, and *Trypanosoma Lewisi* of the rat; whereas from such varieties as these the pathogenic types, *T. brucei*, *T. equiperdum*, etc., and finally *T. gambiense*, the cause of sleeping sickness, and *T. cruzi*, the cause of trypanosomiasis Americana in man, may have originated.

The parasitic habit and pathogenic properties of these blood parasites may be traced through evolution and adaptation to the new environment. Thus the saprozoic crithidia and herpetomonas in the intestine of a biting insect, reaching the salivary glands or proboscis, could easily inoculate a vertebrate during feeding; and although primarily they may be destroyed in the new environment, in time they become adapted to live in the blood as parasites (*T. lewisi*), finally becoming pathogenic (*T. brucei*, *T. gambiense*). The fact that any parasitic trypanosome, when artificially cultivated in ordinary culture-media, returns to its primitive type (crithidia and herpetomona) may be another argument in favor of its saprozoic origin.

Among the higher forms, the trematodes, for example, we also find all gradations; from the ectoparasites found on the surface of frogs and fish, or on the gills and about the mouth, to the endo-

parasites in higher animals and in man. The nematodes also offer interesting examples of parasitic adaptation. Strongyloides, for instance, was divided into two distinct species: *S. intestinalis*, parasitic in the small intestine, and *S. stercoralis*, saprozoic in the soil. Leuckart showed that both species were succeeding generations of one life cycle, in which the parasitic form (*S. intestinalis*) is merely a female organism derived from the saprozoic female and transmitted in the larval stages to man and animals through the skin (Durn and Mazocchi). A peculiarity about this parasite is that only the female is found in man, a fact that may be due to the death of the male shortly after fertilization, as is the case with trichinella. Some authors believe this worm to be hermaphroditic, the male organs disappearing shortly after performing their function; others regard the organism as a parthenogenetic female. Whichever theory is correct, this nematode presents a low grade of parasitic evolution, since it can adapt itself either to the free living or to the parasitic life, according to the environment. The gradual evolution in nematodes is further illustrated in the life history of ankylostoma, ascaris, and trichinella, respectively, and finally in filaria, which represents the highest degree of parasitic existence.

A similar parasitic evolution also takes place among insects. Thus some hemiptera, originally subsisting on the juices of plants, for instance, in biting for purposes of defense may have acquired the habit of feeding on blood, and thus became gradually adapted, first, to a facultative type, and finally to the obligate type of blood-sucking parasite. The same is true of the flies, the majority of which have a saprozoic existence, but in the larval stage are capable of living as parasites in wounds or in the tissues of animals.

Mode of Dissemination and Transmission.—A review of the life history of parasites discloses the fact that there are numerous means of dissemination and propagation. Generally speaking, in those instances in which the parasitic habit is best developed, the eggs or larvæ are carefully deposited in surroundings appropriate for their development. As, however, the parasitic habit becomes more markedly developed, this maternal instinct may be entirely lost, the eggs or larvæ being deposited indiscriminately, with the result that most of them perish, only a few finding their way into the hosts appropriate for their further development. This wastage is, however, offset by a proportionate overproduction of eggs or embryos. It is probably on this account that, as the parasitic mode of life makes it increasingly difficult for the parasite to secure descendants, the reproductive organs become developed out of all proportion to, and at the expense of, other organs, which latter may remain rudimentary or disappear entirely, as in the case of the tape-worms. It has been estimated that a

single Tænia saginata may in one year produce 150,000,000 eggs, one of which, if successfully deposited in an appropriate host, may generate hundreds or even thousands of segments or reproductive organisms, each capable of producing hundreds of new and fertile eggs.

The parasites whose eggs or embryos are transmitted directly into another host are so few in number that this mode of transmission may be regarded as exceptional. As a rule, the germs, eggs, larva, etc., are discharged from the body of the primary host in the soil or water, from which they find their way to the new host; or they may be taken into the body of a secondary host by another route. In any case they are likely to undergo more or less well-marked developmental changes or metamorphosis prior to their successful entrance into the new host. These changes may consist merely of encystment (ameba, coccidia), or they may represent the sexual cycle of the parasite (plasmodium); or they may result in a more complicated life history with complete metamorphosis (fasciola).

As a rule, blood parasites are transmitted through the bite of a blood-sucking insect, either directly (trypanosoma) or after a complex development in the body of the insect (plasmodium).

According to their mode of transmission, intestinal parasites may be divided into two groups: (1) Those having a thick-shelled egg, as, *e.g.*, trichuris, ascaris, oxyuris, tenia, etc., which do not hatch outside of the body of the host, though the larvæ may develop within the egg, being first set free in the stomach or in the intestine of the new host; and (2), those having a thin-shelled egg, such as ankylostoma and strongyloidos, in which the larvæ hatch outside of the body of the host and enter the new host through the skin or with the food.

It may be said that, as a rule, the parasitic protozoa of the intestinal tract (ameba, coccidia) enter the body of the host in an encysted form; the blood parasites, except Schistosoma, are transmitted by blood-sucking insects (malaria, trypanosomiasis, filariasis), and the nematode parasites of the intestines, except ankylostoma and *Strongyloides intestinalis*, in the larva-egg stage. Trichinella is transmitted from host to host in the embryo stage encysted in the muscle. The cestodes are transmitted both in the embryo-egg stage (oncosphere) and in the bladder-worm stage (cysticercus or plerocercoid); and the trematodes in the miracidial or in the encysted cercarial stages.

Vitality of Parasites.—Some parasites, such as fleas, bedbugs, ticks, etc., may go without food for months, while waiting for the proper host.

Among the protozoa encystment is an effective means of protection, the impermeable cyst-wall preventing dehydration or the entrance of injurious substances from without.

Intensity of Infection.—The degree of parasitic infestment and the action of a parasite upon the host are governed, to a great extent, by individual conditions, and by the surrounding media. Faulty hygienic conditions, improper drainage, etc., and particularly carelessness on the part of the individual, such as neglect to cleanse the hands thoroughly, and laxity as regards the personal hygiene, are potent factors in occasioning infestment and reinfestment by parasites that have a direct development, such as oxyuris. On the other hand, swamps, stagnant water, and stables, by favoring the development of mosquitos and flies, predispose to the occurrence of diseases transmitted by these insects. Suitable temperature and humidity in the temperate zones or in mining regions aid in the development of ascaris, ankylostoma, etc. The eating of raw meat is also a predisposing factor to infestment by tape-worms and trichinella.

Age also plays an important rôle in parasitism; thus children and young animals, regardless of hygienic conditions, are more susceptible to ascaris than are adults and such is probably the case in many other parasitic diseases. The normal resistance of the body is greater in some individuals than in others, and this resistance may be so marked in some cases as to constitute a distinct immunity.

Effect of Parasitism upon the Parasite.—It is well known that a parasitic existence always entails retrograde or atrophic changes in the parasite. Certain structures or organs that would be essential to the free living animal undergo degeneration or may entirely disappear, whereas others that are suitable to the new environment may undergo development. Thus parasites which normally are winged, as in the case of some insects, lose their wings; whereas in others the mouth, limbs, etc., undergo modification or are reduced to mere suckers, hooks, or other appendages for attachment to the host. As a parasite becomes dependent upon the host for its nourishment the digestive system becomes merely rudimentary and may eventually disappear. Thus the nematodes are generally provided with a complete intestinal tract, a structure that is rudimentary in the trematodes and entirely absent in the cestodes.

The most marked characteristic of parasites in general is their proliferative power. It has been estimated as already stated that a single *Tænia saginata* may give rise to 150,000,000 eggs each year; *Filaria medinensis* generates millions of embryos, whereas the vegetative reproduction of *Tænia echinococcus* (in the bladder-worm stage) and trematodes (in the sporocyst and redia stage) is almost unlimited. This peculiarity is of great importance for the perpetuation of the organism, for as the maternal instinct of parasites to lay their germs amid the proper surroundings or within an appropriate host is usually lost, these germs are deposited indiscriminately, with the result that

most of them perish, only a few reaching a place favorable for their complete or partial development.

Effect of Parasitism upon the Host.—The mere presence of few parasites in the body does not necessarily imply that morbid change or metabolic disturbance of importance has taken place within the host, except when their location is such as to impair the function of vital organs, or when the parasite liberates certain products that are toxic in nature. In the majority of instances, however, infestation by parasites gives rise to a variety of local or general pathological changes that are associated with a group of symptoms peculiar to parasitic disease, and due to various agencies, such as (1) toxic action; (2) traumatic action; (3) mechanical action; (4) irritative and inflammatiory action; (5) secondary infection or complications; and (8) probably starvation by impairment of the metabolism of the host.

1. *Toxic Action.*—The products of disassimilation of most parasites are usually poor in toxins, and the toxic symptoms are consequently few and, for practical purposes, of secondary importance. The reaction to the bites of an insect is usually local; the symptoms of filariasis are chiefly mechanical, etc. The rise in temperature in malarial fever is believed to be due to the liberation of toxins by the parasite during sporulation. The sudden and acute gastric and constitutional disturbances in trichiniasis, occurring a few hours after infestation, may be due to the liberation and absorption of the fluid contained in the cysts during the escape of the embryos. The pernicious anemia that accompanies ankylostomiasis and dibothriocephaliasis has been attributed to the absorption of toxic products excreted by the parasites. The sarcocystin liberated by Sarcocystis is said to be very toxic for laboratory animals. All these toxic symptoms, however, although undoubtedly severe in a few instances, are of short duration, mild in character in the majority of cases, and never constitute the chief feature of parasitic diseases.

2. *Traumatic Action.*—The traumatic action of parasites upon the host is illustrated by the effects produced on the skin by the bites of insects and by the penetration of larvæ such as those of strongyloides and ankylostoma; by the ulceration of the rectum and bladder in schistosomiasis, due to the lodgment of eggs in the submucosa; by the ulceration of the intestine in ankylostomiasis, and other lesions produced by intestinal parasites in general.

3. *Mechanical Action.*—The mechanical action of parasites upon the host is one of great importance. Its effect is well shown in the obstructive symptoms occurring in filariasis due to stasis of the lymph, which leads to lymphedema, hyperplasia of the skin (Fig. 1), and elephantiasis. It is also demonstrated by the obstruction of the pancreatic or biliary ducts or of the lumen of the appendix by ascaris or oxyuris

(Fig. 2). The phenomenon of compression of the brain by *Cysticercus cellulosæ* and the obstruction of the lumen of the capillaries of the brain, sometimes seen in malaria, are well-known examples of the grave



FIG. 1.—Section of the skin from a case of elephantiasis of the leg showing chronic inflammation of the subcutaneous tissue, *A*; hyperplasia of the epithelium, *B*; with formation of pearly bodies, *C*.

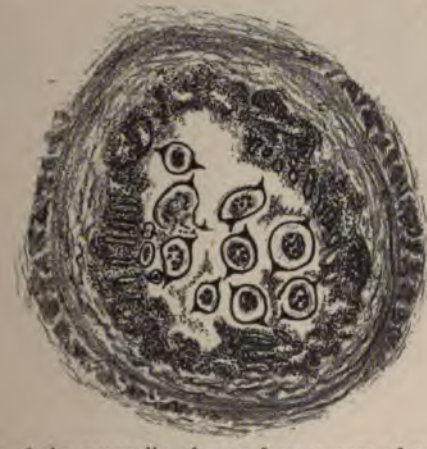


FIG. 2.—Section of the appendix of man from a case of appendicitis due to the lodgment of *Oxyuris vermicularis*. Sections of the parasites are shown in the lumen of the appendix.

consequences that the mechanical action of parasites may exert upon the host (Fig. 3).

4. *Irritative and Inflammatory Action.*—The presence of a parasite in an organ or in the tissues of the host, as a rule, is the cause of an

irritation and a more or less intense chronic inflammation, which may give rise to fibrosis, encapsulation and encystment of the parasite, or to hyperplastic changes, with the formation of a tumor-like growth.

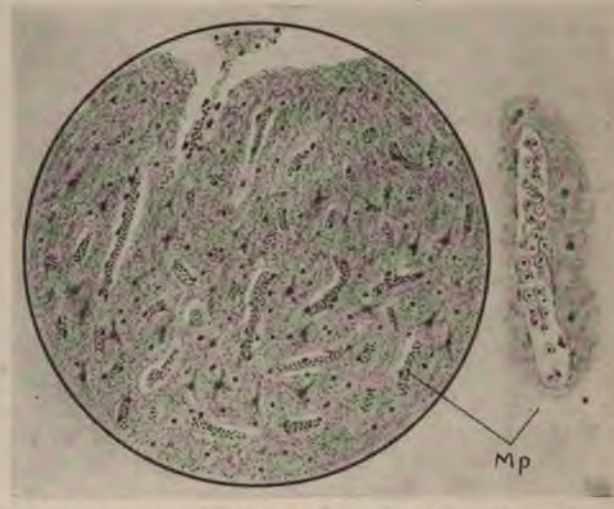


FIG. 3.—Section of human brain showing the malaria parasites, *Mp*, lodged in the lumina of the capillaries.



FIG. 4.—Inguinal lymphatic gland of man from a case of chronic filariasis showing fibrosis and atrophy of the lymphoid tissue.

(Plate II). In some cases the lesion is merely local, and is limited to the area surrounding the parasite; in other cases it may gradually extend until the entire organ is involved or it may even become generalized.



PLATE II.—Stomach of a badger (Taxidea taxis) infested with *Physaloptera turgida* showing the parasite *P*, attached to the mucous membrane, and a tumor-like mass at *T*, caused by the irritation of the organ by the parasites.

As typical examples of irritation and chronic inflammatory lesions in parasitic affections may be mentioned the chronic ulceration of the intestines in amebic or schistosomic dysentery; gastro-intestinal

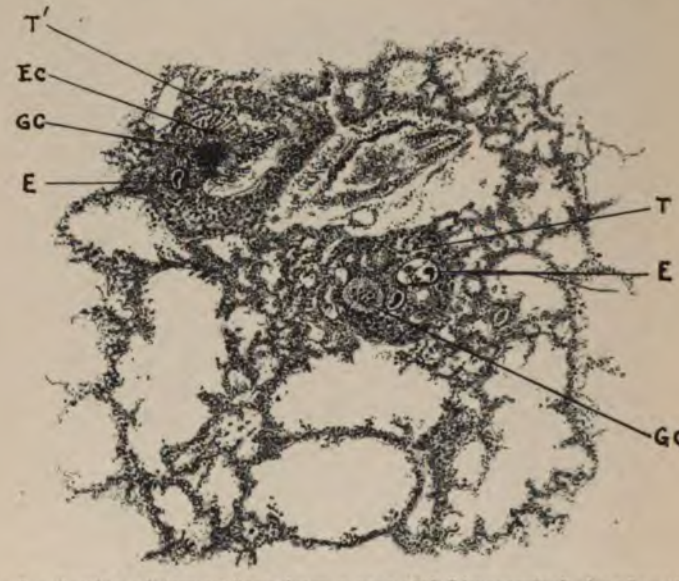


FIG. 5.—Section of human lung from a case of Schistosomiasis showing the formation of typical tubercles, *T* and *T'* caused by the irritation of the eggs of the parasite, *E*, on the lung tissue. *Gc*, giant cells; *Ec*, proliferated epithelioid cells.

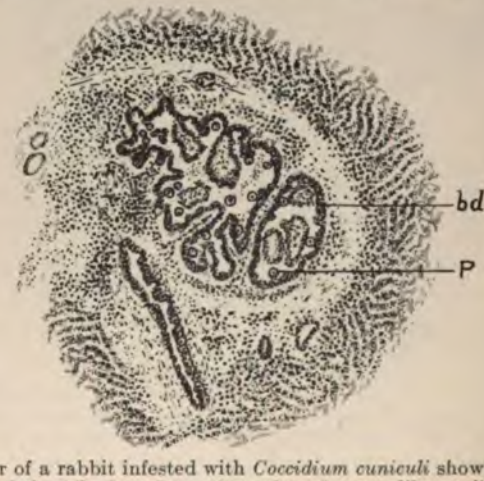


FIG. 6.—Liver of a rabbit infested with *Coccidium cuniculi* showing encysted forms *P*, in the lumen of the bile duct *Bd*. Note the adenoma-like proliferation of the bile duct caused by the parasite.

disturbances seen in ankylostomiasis and in other parasitic affections of the intestine; the chronic bronchitis and formation of tubercles in paragonimiasis and schistosomiasis of the lungs (Fig. 5 and

Plate III); the biliary cirrhosis and adenoma-like proliferation of the bile-ducts produced by *Fasciola hepatica* and *Coccidium cuniculi* (Fig. 6).

Treponema pallidum furnishes a typical example of the gradual extension of an affection from an external focus to the internal organ. In the acquired variety of syphilis the lesion appears first at the site of infection, in the form of a chancre; later, in the secondary stage of the disease, the infecting agent becomes disseminated throughout the body; and in the final or tertiary stage it may give rise to general fibrosis of the internal organs and to arteriosclerosis. In the congenital form of syphilis the lesions involve the entire body.

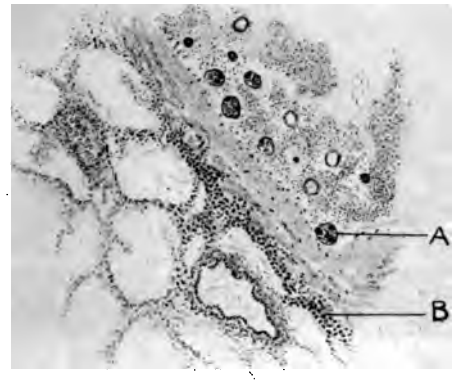


FIG. 7.—Bronchial abscess from a case of Paragonimiasis in man showing the eggs of Paragonimus *A*, in the cavity of the abscess and a peribronchial cellular infiltration *B*.

5. *Secondary Infections or Complications.*—The presence of a parasite in proximity to the normal cavities of the body, in the lumen of the intestine, or in such organs as the lungs, liver, etc., communicating directly or indirectly with the exterior, is a constant menace to the host. Not uncommonly the parasite may cause destruction of the surrounding tissue or ulceration of the part, as the case may be, and a resulting bacterial infection may ensue. This is well illustrated in cases of extensive ulceration and general infection in ankylostomiasis, in acute inflammation and abscess formation in the lung in paragonimiasis, and in similar conditions in the liver caused by the presence of *Fasciola hepatica.*

In general it may be said that the mere presence of the parasite in the body, is not a matter of immediate danger to the patient, unless the organisms are found in exceptionally large numbers or are lodged in vital organs. In most parasitic infestments death when it

occurs is due either to the mechanical action of the parasite upon a vital organ or to secondary bacterial infection.

6. *Starvation.*—It is a common belief among the laity that a person infested with tape- or round-worm eats more than he would normally for he must supply food for the parasite as well as for himself. A voracious appetite is, therefore, believed to be one of the symptoms of such infestation. All parasites derive their sustenance from the host but the latter does not, as a rule, suffer in consequence of such loss. It cannot be denied, however, that blood-sucking insects actually feed upon our blood, and it is conceivable that the malarial parasite, by destroying large numbers of erythrocytes, may be responsible for the improper oxidation of the tissues, and give rise to metabolic disturbances, thus accounting in part for the rapid emaciation and general

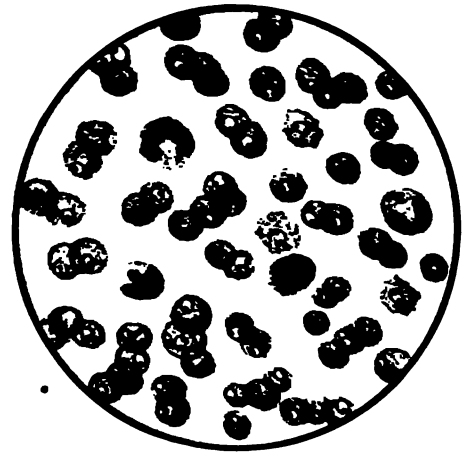


FIG. 8.—Blood preparation showing over 50 per cent. of the erythrocytes parasitised by the ring form of the malaria parasite (subtertian).

weakness so commonly seen in the acute stage of those cases of malarial fever in which over 50 per cent. of the erythrocytes are parasitized (Fig. 8).

Pathogenesis in Parasitic Infestments.—Bacterial diseases in general are characterized by sudden onset and run an acute course that ends either in complete recovery or in death. Immunity against the infecting disease follows in most cases, and unless complications set in, no traces of the infection remain. Conversely, diseases caused by animal parasites are, with few exceptions, chronic disturbances; their onset is slow, their course is protracted, and complications are prone to develop; their prognosis is uncertain. Complete recovery is rare, and, as in the majority of instances no immunity is conferred, the patient is always susceptible to reinfestation. As the parasite is the source of inflammatory changes, chronic and permanent pathologic dis-

turbances of the part or the organ affected may occur, or lead to destruction of tissue, with the result that a fatal bacterial infection may take place at any time.

In malarial fever, for example, the onset is slow, and if the case goes untreated or is improperly managed, the course is generally protracted and of uncertain prognosis. The chronic pathologic disturbances that affect the internal organs, and the profound alteration in the blood which usually occurs, may bring about a fatal termination. After a time—weeks or months—the disease becomes chronic, the fever subsides, and the number of parasites in the blood may be so reduced as to render their detection in the peripheral circulation difficult, or they may eventually disappear, and the patient assume a normal appear-

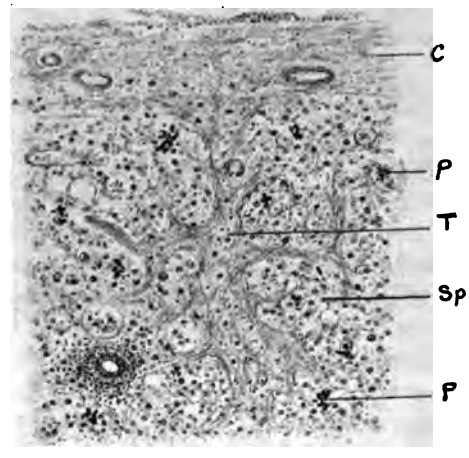


FIG. 9.—Section of the spleen from a case of chronic malaria showing fibrosis and thickening of the capsule *C*, and trabeculæ *T*, atrophy of the splenic pulp *Sp.*, and a general pigmentary infiltration of hemozoin especially seen at *P*.

ance. The spleen and liver are, however, the seat of chronic disturbances, and are likely to remain permanently enlarged, fibrotic, pigmented and congested (Fig. 9). These disturbances gradually grow worse, and indirectly give rise to organic complications that eventually prove fatal. Death in such cases is, of course, due to the complications.

Defense of the Organism Against Parasites.—In all cases of infection the reaction of the organism is one of defense against the invading parasite. As is known, no portion of the body is sterile: a certain number of bacteria must necessarily constantly penetrate our normal barriers—mucous membranes, skin, etc. As a result, microörganisms, although in small number, are always present in the blood and tissues of the body, but under normal conditions they are destroyed by phago-

cytosis, physicochemical agencies, etc., and the normal balance is thus maintained. It is only when this balance is disturbed, that is, when the resistance of the organism is lowered, or when the number of bacteria present overbalances this antagonistic power, that the phenomena of infection or disease are manifested.

The same is true of animal parasites. In the case of *Endamœba histolytica* there is no doubt that the occasional amebæ that escape the destructive action of the stomach may pass through the intestinal canal without giving rise to dysentery, and that in those districts, in which dysentery is endemic, a certain number of the protozoa may be present in the intestine for some time without causing any disturbance in the host.

The same is true concerning the entrance of a few sporozoites of the malarial parasite into the blood with the bite of the mosquito. Of the number of ankylostoma and trichina larvæ that may gain entrance to the system, only a small percentage succeed in reaching the duodenum, and if their number is very small, they would be incapable of setting up an appreciable disturbance. Not uncommonly, however, the infestment is in sufficient intensity to break down the natural defense of the organism, with the result that the normal balance is no longer maintained, and symptoms of disease are manifested. The means by which the organism defends itself against parasitic infestment are 1 mechanical agencies; 2 thermogenic phenomena; (3) physicochemical and organotropic agencies; 4) humoral phenomena; (5) histogenic reactions, and 6 cellular phenomena.

1. *Mechanical Agencies.*—The skin and mucous membrane of the normal cavities of the body act as the most effective barriers against invasion. An abrasion of the mucous membrane or of the skin is essential for the entrance of *Treponema pallidum*, and wounds on the delicate mucous membrane of the nose, conjunctiva, etc., are factors that predispose to the development of diptera larvæ in these localities. The peristaltic action of the intestine in diarrhea or the effort of vomiting may cause the mechanical expulsion of intestinal parasites (ascaris, tape-worms, etc.).

2. Thermogenic Phenomena. Just as birds are more or less immune to anthrax because their normally high temperature is detrimental to the anthrax bacillus, so man is immune to a number of bacterial and parasitic diseases peculiar to animals of lower organization that have a body temperature lower than that of man. A certain degree of heat is therefore essential to the life of an organism, and this explains why a body temperature is favorable for the existence of the parasite as found in man, and also why a rise in body temperature of a few degrees for a certain length of time must have a detrimental effect upon the parasite. The high temperature that is common in all in-

fectious diseases (typhoid, scarlatina, measles, pneumonia, small-pox, etc.), although injurious to the patient, must undoubtedly exert a detrimental action upon the viruses of these diseases. It is probable that this is also the case with all protozoan and metazoan parasites; therefore, the thermogenic activity of the body undoubtedly serves as one of the most efficient means of defense against the invading organism. This factor may also explain the spontaneous expulsion of intestinal parasites (tape-worms, ascarides, etc.) during the febrile stage of an attack of small-pox, measles, typhoid fever, etc.

3. *Physicochemical and Organotropic Agencies.*—The chemistry of the body, or of the part involved, bears an important relation to the life of the parasite. The acidity of the stomach, it is known, exerts a germicidal action against bacteria and higher organisms, and this explains, perhaps, the rarity of trichiniasis in dogs and in most carnivorous animals in whom the acidity of the gastric secretion is normally high.

That the germicidal action is due to the hydrochloric acid present may easily be proved in vitro. Artificial cultures of trichina embryos, grown in chemically produced gastric juice, perish within a few hours after their escape from the cyst, but if removed to a neutral or an alkaline medium, or to simple physiologic salt solution, they may live for several days.

The fact that trichinella and ankylostoma inhabit by preference the duodenum, whereas, ascaris prefers the lower part of the small intestine; oxyuris the small intestine when young and the large intestine when grown, and trichiuris selects the cecum, etc., and also that none of these parasitize the stomach, shows quite clearly the chemotropic relation that exists between the parasite and the surrounding medium.

The fact that, in the course of gastro-intestinal disturbances, the chemistry of the intestinal contents undergoes marked changes, explains the spontaneous expulsion of intestinal parasites in not a few instances; and certain chemical alterations in the body in general that occur during the course of constitutional diseases perhaps also explains the occasional presence in man of parasites that are peculiar to the lower animals.

That certain organs or tissues are favorable to, whereas others are antagonistic to, the life of a parasite, is clearly seen in the preference which *Fasciola hepatica* displays for the liver; paragonimus for the lung; filaria for the lymphatics; plasmodium and trypanosoma for the blood, etc. Since a parasite perishes when it is transplanted experimentally to a place other than that which it commonly inhabits, is proof of the unfavorable action of certain organs and tissues on the life of the parasite. This fact is not, of course, a matter of chance,

but is due to the chemistry of the part; in other words, it is occasioned by the presence of certain substances essential or prejudicial to the proper development of the parasite. Nevertheless other factors, *e.g.*, mechanical agencies, may play a rôle in certain cases, and explain such circumstances as the absence of trichinella embryos from the heart muscle.

Occasionally a parasite may be found distant from its normal habitat; thus *Fasciola hepatica* may parasitize the lung, *Paragonimus westermanni* may be found in the liver, etc., this occurs, however, only in exceptional cases, and usually when the infestment is extremely marked in the organs normally parasitized by these organisms. It is conceivable, for instance, that the larvæ of *Paragonimus westermanni*, on reaching the circulation, are distributed by the action of the heart to all portions of the body, the greatest number being retained in the capillaries of the lung; a few passing through the pulmonary circulation and reaching the left heart may be carried to the liver through the hepatic artery, whereas others may be carried to still more distant parts of the body. As a rule, the organisms transported to the unusual situation perish, but the chemistry of the part may at times be so altered by other diseases as to favor development.

4. *Humoral Phenomena.*—All infections have a tendency to produce more or less alteration and change in the body, with the appearance, in the blood and humors, of certain substances known as antibodies or *amboceptors*, which are antitoxic or defensive in character. These antibodies may take the form of precipitins (hydatid cyst) or agglutinin (trypanosomiasis), etc., and though their action is almost inappreciable in most cases, the natural disappearance of *Trypanosoma lewisi* in the rat, of *Spirochæta recurrentis* in relapsing fever, and of *Treponema pertenue* in man, and the resulting immunity conferred after recovery from infection by these organisms, are illustrations of the antagonistic action of these antibodies.

5. *Histogenic Reactions.*—A parasite lodged in any portion of the body is a source of irritation that gradually gives rise, in most cases, to a lymphocytic infiltration and finally to a hyperplasia of fibrous tissue around the parasite. In some instances this overgrowth of fibrous tissue is so complete as to constitute a distinct encapsulation and encystment, with, not uncommonly, calcification. These histogenic changes are defensive in character, restricting the action of the parasite and preventing damage to the adjacent tissues.

In those instances in which encapsulation is complete and calcification has taken place, the parasite is, as a rule, dies, but it is a moot question whether the calcification of the cyst is the cause or the effect of the death of the parasite. The encystment of the liver fluke, and more especially of tape-worm larvæ, trichinella, and sarcocysts, are

typical examples of this histogenic phenomenon as a means of defense on the part of the organism (Fig. 10).

6. *Cellular Phenomena.*—The cellular defense of the organism against infection is best illustrated in the much discussed phenomenon of phagocytosis. Phagocytosis is the property of certain cells of the body to ingest, destroy, and digest the invading microörganisms or to neutralize and modify their products. The phenomenon is especially marked in the leukocytes (microphages) and endothelial cells (macrophages), although almost any cells of the body may, under certain conditions exhibit some degree of phagocytic activity (Fig. 11).

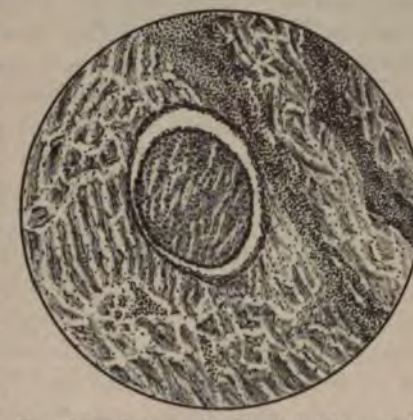


FIG. 10.—Sarcocystis rileyi in the muscle of a wild duck.

Phagocytosis has been observed in nearly all bacterial infections, and there are evidences that it may also occur in protozoan diseases.

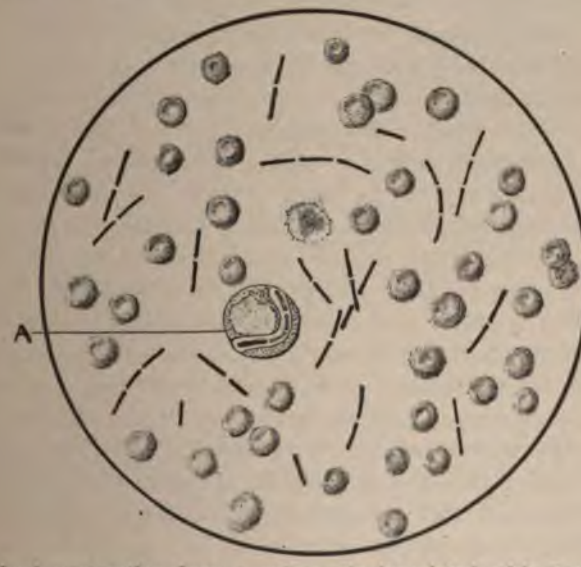


FIG. 11.—Blood preparation from a guinea pig inoculated with *Bacillus anthracis*, showing the bacilli phagocytized by a leucocyte *A*.

One of the most characteristic cytogenic activities of the body is shown in the increase in eosinophiles in the blood in all metazoan infestations. That this increase is related to the presence of the

metazoa is proved by the fact that the eosinophiles are more numerous not only in the circulating blood, but also in the tissue or in the region adjacent to the parasite, forming what may be called an "eosinophilic infiltration." Regarding the nature of this phenomenon but little is known; it is probable that, by neutralizing the injurious products, given off by the parasite, it serves as a means of protection.

Another cytogenic phenomenon of the organism against the parasite and its activity is observed in those cells that come into contact with the parasite; thus the columnar epithelium of the bronchus is changed into squamous epithelium by *Paragonimus westermanni.* (Plate III.)

Ultimate Fate of Parasites.—The disappearance of a parasite from the host may be effected in three ways: (1) By artificial means (medication); (2) by spontaneous expulsion, which, as previously stated, frequently occurs in the case of intestinal parasites during the course of infectious fevers, more especially, when these are accompained by a high temperature, gastro-intestinal derangements, or other disturbances that may cause profound changes in the chemistry of the intestine; and (3) actual death of the parasite. The disappearance of the parasite, however, is not necessarily accompanied by the absence of other symptoms due to complications. Thus the elephantiasis of filariasis; the hyperchromatosis, enlarged spleen, and secondary anemia of malarial fever; the ulceration and stenosis of the colon in dysentery; and the anemias in ankylostomiasis, etc., are complications that tend to persist for prolonged periods or even indefinitely after the removal of the parasite.

With the exception of those cases in which the parasite reproduces vegetatively in the host, as in malarial fever and in coccidiosis, or in those instances in which the larval stage is preserved for a long time (trichinella, hydatid cyst), it may be said that the duration of life of a parasite, excepting perhaps the cestodes, is limited and undoubtedly much shorter than that of the host. Thus, the life span of an adult trichinella in the intestine is only a few weeks for the male and two or three months for the female; *Strongyloides intestinalis* may not survive for more than one or two years; and ankylostoma, ascaris, trichuris, and *Filaria bancrofti* may perish in possibly less than five and not more than ten years. The trematodes apparently have a shorter life than the nematodes, but the cestodes may live for a very long time—perhaps during the entire life of the host.

As experimental work and observations along this line are lacking, the foregoing statements are merely theoretic. When the life duration of parasites in the host is more clearly understood, the profession will be better fitted to cope with and control the infection and by employing prophylactic measures shorten the course of most of the para-

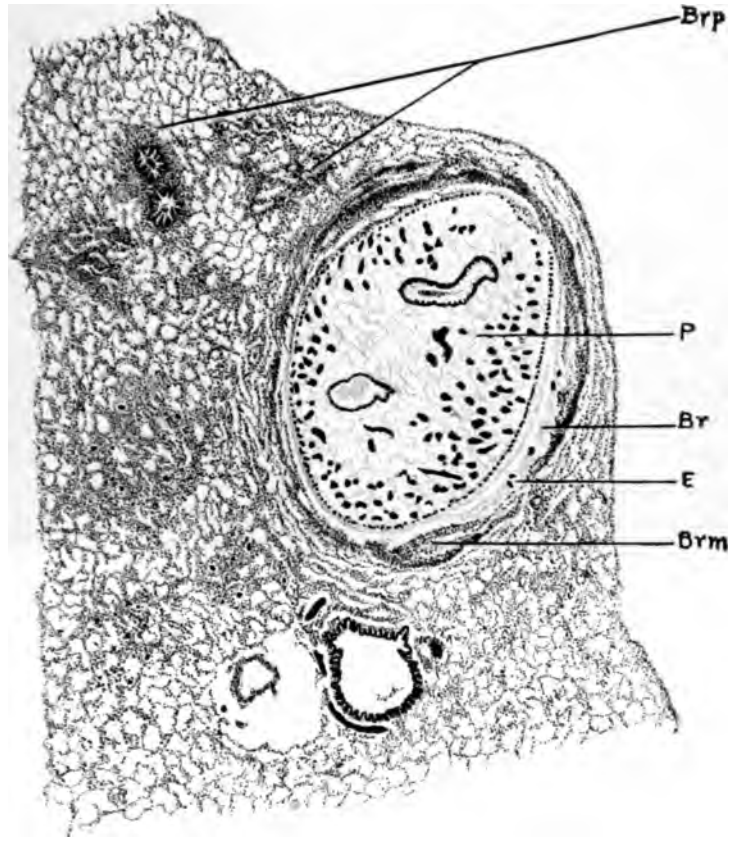


PLATE III.—Section of the lung of a wild cat infested with *Paragonimus westermanii* showing the parasite, P, lodged in the cavity of a distended bronchus, Br. Note the bronchopneumonic areas, Brp, surrounding the bronchus and the hyperplasia of the bronchial mucosa, Brm, caused by the irritation of the tissue by the parasite. Few eggs, E, are seen near the wall of the bronchus.

sitic diseases. It is well known that trichuris infestment may persist during the entire life of an individual, and the same may be said of ankylostoma, filaria, and other similar affections. This is not, however, due to the fact that these parasites are capable of living for so many years, but to the subsequent reinfestment and constant introduction of new parasites in the host.

It is not the primary infestment, but the subsequent reinfestments that are responsible for the grave disturbances in parasitic diseases. It is conceivable, for instance, that a single bite of a mosquito carrying the malarial parasite may not be capable of transmitting the disease, unless a large number of sporozoites are introduced at the same time. This is true of all diseases of man, whether bacterial, protozoan, or metazoan in origin. The well-known benefit that accrues from a change of climate in malarial fever and the removal of the patient to a non-malarial locality, are nothing more than prophylactic measures against reinfection. The same principles applied to early cases of filariasis, schistosomiasis, paragonimiasis, etc., would probably lead to a successful result in the treatment of these diseases, which are generally regarded as incurable since in this way reinfestment is prevented, the existing parasites would in time disappear, dying, as it were, of old age. These principles as applied to individual parasites will be discussed in subsequent chapters.

Pseudoparasitism.—During the course of our routine examinations we not uncommonly encounter certain objects, artefacts, or detritus that bear a strong morphologic resemblance either to eggs or to parasites in different stages of development. To such objects the name pseudoparasites has been given.

On closer observation these pseudoparasites will be found to be made up of vegetable detritus, such as wood fibers, hairs, starch-grains, pollen grains, etc., which may resemble an egg; or they may consist of vesicles of the pulp of an orange, seed, muscle-fiber, casts of the intestinal mucosa, or blood-clots, which may resemble adult worms.

In some cases live organisms, usually larvæ of various kinds, but occasionally higher creatures, such as lizards, are brought by patients with the history that they were passed with the feces, urine, etc. Not uncommonly the patient may give a distinct history of symptoms peculiar to some parasitic disease.

Among the organisms found in cases of pseudoparasitism are diptera larvæ, myriapods, nematodes, etc. Occasionally these organisms may be passed alive with the urine, feces, or vomitus, and it is possible that they represent a kind of facultative parasitism in the transitional stage of parasitic evolution.

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PART II

PROTOZOA

CHAPTER III

GENERAL CONSIDERATION OF PARASITIC PROTOZOA

Definition.—Morphology and Structure: The Cytoplasm; The Nucleus; The Rhizoplast; The Vacuoles.—Motility.—Reproduction.—Life History: Asexual and Sexual Reproduction; Parthenogenesis and Etheogenesis.—Mechanism of Transmission.—Pathogenesis.—Classification.

Definition.—Protozoa are primitive unicellular organisms found abundantly in nature, either living free or existing as parasites on higher organisms. They reproduce asexually—by fission (schizogony), budding, fragmentation, spore formation, etc.—and sexually (sporogony) or through rejuvenation by conjugation.

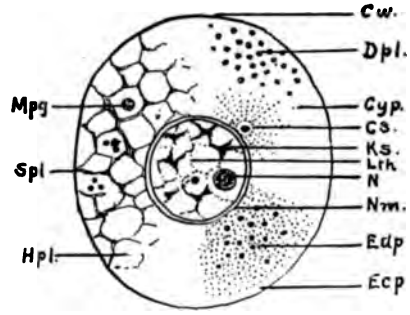


FIG. 12.—Diagram of the cell. *Cw*, cell wall; *Dpl*, deutoplasm; *Cpl*, cytoplasm; *Cs*, centrosome; *Ks*, karyosome; *Lth*, linen threads; *N*, nucleolus; *Nm*, nuclear membrane; *Edp*, endoplasm; *Ecp*, ectoplasm; *mpg*, metaplastic grains; *Spl*, spongioplasm; *Hpl*, hyaloplasm.

Morphology and Structure.—The protozoan parasites usually present a more or less distinct and constant form although they are for the most part ameboid at a certain stage of their development. Structurally these unicellular organisms differ in no essential from the common cell type (Fig. 12) and consist of a cytoplasmic or achromatic substance and a nuclear or chromatic substance. The organisms also possess vacuoles, pigments, and appendages in the form of pseudopodia, cilia, or flagella, which serve as organs of locomotion.

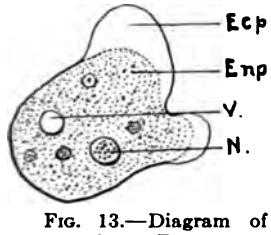


FIG. 13.—Diagram of an ameba. *Ecp.*, ectoplasm; *Enp.*, endoplasm; *V*, vacuole; *N*, nucleus.

The Cytoplasm.—The cytoplasm represents the main bulk of the organism, and is not uncommonly clearly differentiated into an outer portion—the *ectoplasm*—which is clear and hyaline in appearance, and a darker portion—the *endoplasm*—which is made up of cell-sap and cytoplasmic granules (Fig. 13). The latter may be differentiated as *chromidia, volutin, metachromatic*, and *metaplastic* grains. The cyto-

plasm may also contain vacuoles and centrosomes, or may be divided into *archoplasm* and *rhizoplast.*

Chromidia Grains.—The chromidia grains are basic staining chromatic granules found in the cytoplasm, and are derived from cytoplasmic remains. Aggregations of very minute chromatic particles are called *chromidiosomes.* It is a generally accepted fact that the chromidiosomes of the nucleus are formed by the grouping together of these chromidia grains. In this respect the nucleus may be regarded as cytoplasmic in origin, the chromidia grains representing an intermediate stage in the nuclear evolution. In such primitive organisms as the spirochetes and treponema, in which no nucleus is demonstrable,

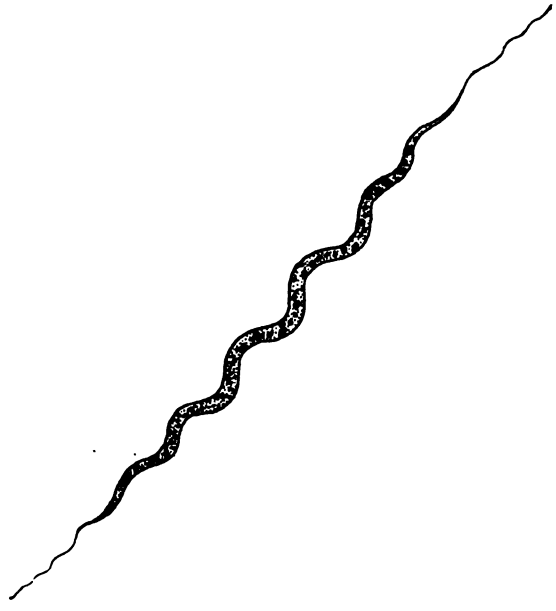


FIG. 14.—Diagram of a Treponema showing chromidial grains.

the chromatic substance is said to be in the chromidiosome or chromidial stage, thus forming a so-called diffused nucleus (Fig. 14).

Volutin Grains.—The volutin grains are substances composed of nucleinic acid in combination, and probably represent reserve food material; they stain with the basic dyes.

Metachromatic and Metaplastic Granules.—The metachromatic granules may be regarded as metabolic products of the chromatin. The metaplastic granules are probably cytoplasmic in origin.

Centrosomes.—The centrosomes are minute chromatic granules usually situated outside of the nucleus, close to the nuclear membrane. They are surrounded by a clear cytoplasmic zone called the *archoplasm.*

Rhizoplast.—The rhizoplast consists of minute delicate cytoplasmic

strands surrounding that portion of the flagellum of trypanosomes that penetrates into the cytoplasm (Fig. 15).

Vacuoles.—The vacuoles are usually clear spaces, more or less regular in outline, seen within the cytoplasm. Two varieties are seen—contractile vacuoles and food vacuoles. The contractile vacuoles are few in number—generally one or two; they are clear, and, as a rule, have a constant shape, size, and location; they are primarily osmotic, respiratory, and excretory in function. The food vacuoles are generally numerous, and may be clear or granular and dark. They vary in shape, size, and location, and receive the acids and ferments secreted by the cytoplasm for the digestion of food. When stained with methyleosin, they may take the basic or the acid stain, depending on the nature of the food and the degree of digestion. When digestion is completed the vacuoles appear as clear spaces, usually regular in outline, and having some detritus in the center.

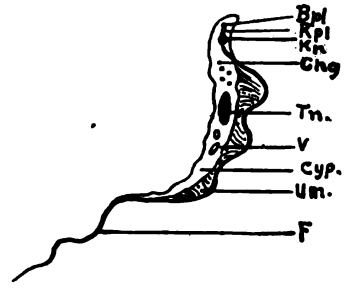


FIG. 15.—Diagram of a Trypanosome. *Bpl.*, blephoroplasta; *Rpl.*, rhizoplast; *Kn.*, kinetonucleus; *Chg.*, chromidial grains (micronucleus?); *Tn.*, trophonucleus; *V*, vacuoles; *Cpl.*, cytoplasm; *Um.*, undulating membrane; *F.*, flagellum.

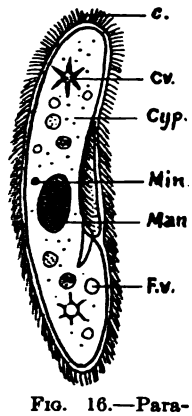


FIG. 16.—Paramœcium caudatum. *C.*, cilia; *Cv.*, contractile vacuole; *Cp.*, cytoplasm; *Min.*, micronucleus; *Man.*, macronucleus; *Fv.*, food vacuoles.

The Nucleus.—The nucleus is that specialized, more or less chromatic substance, seen in the endoplasm. It is usually single, as in the rhizopods, constant in location and shape, and regular in outline. In some species, *e.g.* (the trypanosomes) it occurs in two forms: (1) As a relatively large structure, the *macronucleus, trophonucleus,* or nutrition nucleus; and (2) as a *kinetonucleus,* which is usually very small, and has also been called a blepharoplast. In addition a third variety—the *micronucleus,* or reproductive nucleus—may be present. The micronucleus differs markedly from the trophic and the kinetic nucleus, for the macronucleus is trophic and the kinetonucleus is kinetic in function, whereas the micronucleus is purely reproductive, a typical example being the heterokaryota (Paramesium). The arrangement of several nuclei in chains is peculiar to some of the ciliates (Fig. 16).

The nucleus is generally made up of two substances, one chromatic and the other achromatic. The chromatic substance is rich in nucleic acid, which, having an affinity for the

basic stains, appears blue or of dark hue when stained with methyl-blue or hematoxylin. The achromatic substance is the nuclear sap or *enchylema*. It is semiplastic or liquid in consistence, and bears the same relation to the nucleus that the cell-sap does to the cytoplasm. This achromatic substance may undergo condensation and form achromatic granules or, as they are called, "linin threads," which constitute the framework of the nucleus and upon which the chromatic substance is suspended.

The nucleus in its simplest form is termed the *protokaryon;* this consists merely of an aggregation of chromatic particles, *the chromidia,* into a single mass, known as a *karyosome,* which lies in a delicate achromatic network of linin within a vacuole filled with nuclear sap enchylema. A nucleus of this type has no definite nuclear membrane. The vesicular nucleus, which is a more specialized type, has a distinct nuclear membrane that separates it from the cytoplasm. Within this nucleus are found chromatic structures and chromatin, suspended in an achromatic network of linin.

The *nucleolus* is rarely seen in protozoa, but when it is present, is derived from the nuclear sap. It occurs in the form of lumps of *plastin,* combined with chromatic substances called *karyosome, endosome,* or "Binnenkörper."

Motility.—Protozoa are more or less motile, locomotion being accomplished by means of pseudopodia, cilia, or flagella. Under unfavorable conditions, such as lack of proper food, desiccation, irritation, subnormal temperature, etc., the organisms may become quiescent or lose their motile power. Under such circumstances they invest themselves with an envelop or membrane and become encysted.

Reproduction.—In protozoa reproduction takes place either asexually or sexually.

Life History. Asexual Reproduction.—This form of reproduction may take place by—(1) Binary fission; (2) gemmation, (3) plasmotomy; or (4) spore formation—by amitotic or by mitotic division.

Amitosis.—In its simpler form the amitotic division consists merely in a primary elongation of the nucleus, followed by corresponding constriction of the cytoplasm and final division and separation into more or less equal halves (Fig. 17).

Mitosis.—Mitotic division consists of a primary division of the nucleus into two parts, followed by a similar division of the cytoplasm. There are four types of mitotic division: (*a*) Chromidial fragmentation; (*b*) promitosis; (*c*) mesomitosis; (*d*) metamitosis.

(*a*) *Chromidial Fragmentation.*—This is the simplest type of mitotic division, and consists in fragmentation of the nucleus into several chromidia granules, followed by a rearrangement of the chromidia

into two distinct nuclei. This is later followed by division of the cytoplasm, and finally by the formation of two distinct cells (Fig. 18).

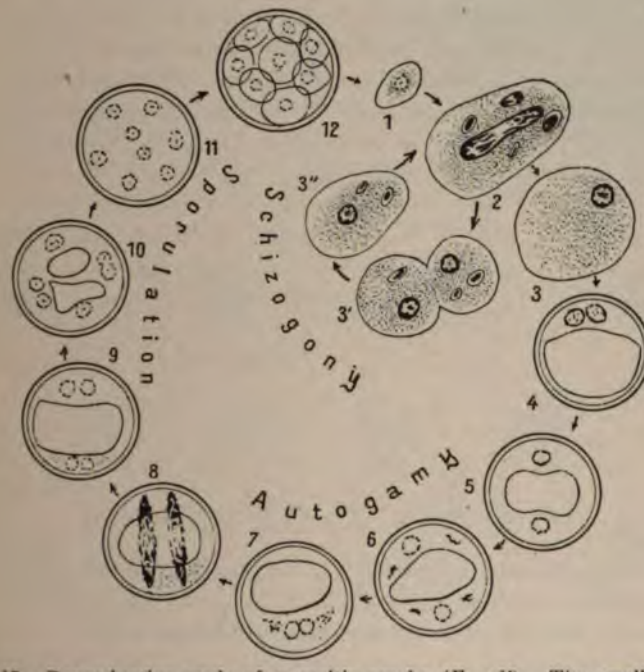


Fig. 17.—Reproductive cycle of parasitic ameba (*E. coli*). The small circle indicated by 1, 2, 3, 3′ and 3″ indicated multiplication by schizogony or binary division. The large circle indicated 1–12, the sporogeny or sexual cycle. The ameba having arrived at its full size (3) becomes encysted (4). The nucleus then divides into two (5), each half expels a small fragment of nuclear material (6), and when this has been effected, they conjugate (7) forming a synkaryon. The synkaryon then divides into two, into four, and then generally into eight (8–9–10–11–12) when the cyst ruptures, the spores are liberated (1) and both cycles are again started. (*After Wenyon in McFarland.*)

(*b*) *Promitosis.*—Promitosis represents a more advanced type of mitotic division. In this form the centrosome divides into two portions, and is followed by division of the protokaryon type of nucleus into two karyosomes, which finally separate into two daughter nuclei.



Fig. 18.—Mitosis showing chromidial fragmentation.

This is followed by division of the cytoplasm and finally by the formation of two distinct cells. In promitotic division a nuclear spindle is formed but no equatorial plates are seen. The chromosomes are scattered through the spindle, and finally separate into two daugh-

ter nuclei. In more advanced types an equatorial plate may be formed.

(*c*) *Mesomitosis.*—This form of mitotic division takes place in a nucleus that is rich in chromatin. Reduction of chromosomes, equatorial plate formation, and perfect karyokinetic figures are the result. The whole process takes place within the nuclear membrane.

(*d*) *Metamitosis.*—Metamitosis is similar to mesomitosis, except that the polar caps of *archoplasm* (the clear space around the centrosome) also assist in the division (Fig. 19).

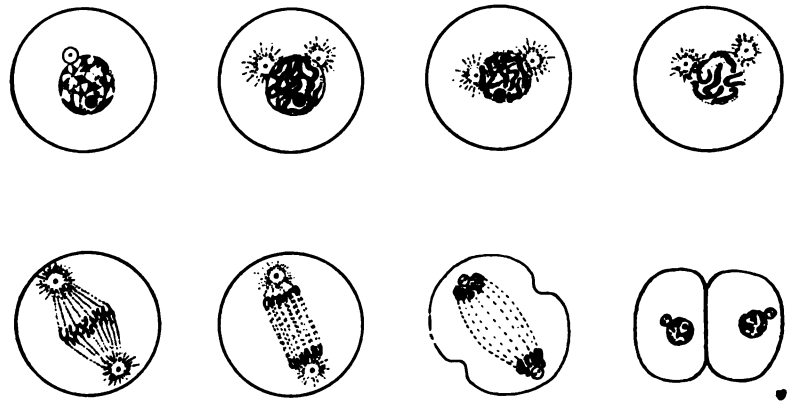


FIG. 19.—Mitosis with spindle formation.

1. *Binary Fission.*—Binary fission consists in the division of the nucleus, at times by amitosis, followed by division of the cytoplasm into more or less equal halves, and the final formation of two young parasites (Fig. 17).

2. *Gemmation.*—In this form of reproduction by budding the nucleus usually divides by mitosis into two or more nuclei, each of which becomes surrounded by small masses of protoplasm. Gemmation may be exogenous or endogenous.



FIG. 20.—Exogenous gemmation.

(*a*) *Exogenous Gemmation.*—In this variety of gemmation the newly formed nucleus travels to the periphery, becomes surrounded by protoplasm, and, by budding, separates externally from the mother cell (Fig. 20).

(*b*) *Endogenous Gemmation.*—The newly formed nuclei do not wander to the periphery of the parent parasite, but remain in the cytoplasm, a portion of which becomes differentiated around each

nucleus. Endogenous gemmation may, therefore, be said to be a process of internal budding, in which the budding area is inclosed in a brood-sac in the mother cell. To this condition the name *pansporoblast* has been applied. In those cases in which the entire organism forms a pansporoblast (as in Sarcosporidium) the whole cell represents only the pansporoblast (Fig. 21).

3. *Plasmotomy.*—This term is applied to the division of the cytoplasm of a multinuclear parasite into two or more masses, which later may or may not reproduce by spore formation.

4. *Spore Formation.*—Sporulation, more than a type of single internal gemmation, may be regarded as a process of pansporoblastic formation. It may take place during growth or the trophic phase (*Neosporidia*), after a short quiescent stage, or following the end of the period of growth (*Telosporidia*). In any case spore formation is a distinct phase of the life cycle.



FIG. 21.—Endogenous gemmation, pansporoblast.

The growth and sporulation of *Telosporidia* consist of three phases: first, the *trophozoitic stage,* in which the parasite imbibes nutriment and increases in size; hence, it is called a *trophozoite;* second, the quiescent or fully grown stage—*schizont*—in which no nutriment is absorbed; and third, that stage in which the nucleus and cytoplasm divide into a certain number of small asexual spores or *merozoites* (Plate VI).

The merozoites represent the asexual reproduction of the parasite in a given host, but are not the means of transmission to another host. The parasites enter a new cell in the host in which they are formed, develop into a trophozoite, then become a schizont, undergo division, and merozoites are formed and the cycle is repeated. This asexual life cycle is termed the schizogonic cycle, or *schizogony.*

Sexual Reproduction.—Owing to the peculiarity of the life cycle of the parasite, together with unfavorable changes in the environment, as when chemical changes in the tissue of the host take place or when there is insufficient food material to supply the demands of the parasites produced by asexual reproduction, etc., specialized sexual forms, called *gametocytes,* are produced. These are of two varieties—the *microgametocyte,* or male cell, which is rich in chromatin, and the *macrogametocyte,* or female cell, which is poor in chromatin.

Sexual reproduction takes place as follows: The nucleus of the microgametocyte divides, either by fission or by spore formation, into three or five nuclei, which travel to the periphery of the cell to form

the beginning of a *microgamete*. The microgamete becomes gradually formed, pushes its way through the surface of the gametocyte, similar to a pseudopod; the gametocyte gradually elongates, carrying with it a corresponding amount of cytoplasm and chromatin; finally it separates from the cell, to become a fully formed microgamete free and mobile in the surrounding medium (Fig. 22). The changes that



FIG. 22.—Sporogony of Plasmodium vivax Grassi and Feletti. Development of the the Microgamete.

1, Young microgametocyte; 2, 3, older forms; 4, fully-grown microgametocyte as seen in the blood of man; 5, division of the nucleus (reduction) in the stomach of an anopheline; 6, nuclei have traveled to the periphery, which has grown out to form the commencement of a microgamete; 7, microgametocyte with three microgametes; 8, a free microgamete. (*After Schaudinn in Castellani and Chalmers.*)

take place in the macrogametocyte consist of maturation of the nucleus, reduction of chromosomes, and the formation of polar bodies (Fig. 23). Conjugation consists in the entrance of the microgamete into the macrogamete. Zogosis takes place by the fusion of the two nuclei and the formation of an individual with the fusion nucleus (*synkaryon*), known as *zygote* or sporont. The zygote takes on the

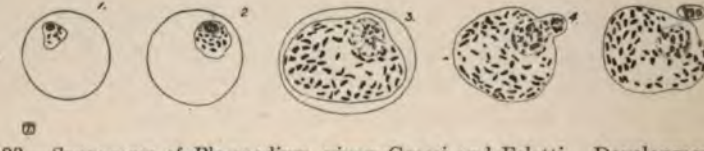


FIG. 23.—Sporogony of Plasmodium vivax Grassi and Feletti. Development of the Macrogamete.

1–3, Young macrogametocytes; 3, fully-developed macrogametocyte in the blood of man; 4, reduction and formation of a polar body in the stomach of an anopheline mosquito; 5, macrogamete and one polar body. (*After Schaudinn in Castellani and Chalmers.*)

form of an elongated body called *oökinete*, which by division gives rise to a *sporoblast*. Finally, by further division and differentiation, the sporoblast gives rise to several *sporozoites*. These, entering a new host, become trophozoites and the cycle is repeated (Fig. 24).

Parthenogenesis and Etheogenesis.—*Parthenogenetic reproduction* (Fig. 25) has been described as taking place occasionally from the macro-

gametocyte of Plasmodium malariæ, and *etheogenetically*, more rarely, from the microgametocyte in *Herpetomonas muscæ*. These modes of reproduction consist in the division of the nucleus of the gametocyte into two portions, one of which degenerates and disappears, whereas the remaining portion forms merozoites and starts the asexual cycle anew. Neither process has been definitely known to take place.

In the life history of protozoa development may be direct, *i.e.*, without an intermediate host, as in the case of coccidia, ameba, etc., or indirect, when a second host is required, as is the case with *Plasmodium malariæ*. In those instances in which it is direct the parasite becomes encysted at some phase of its development, and in this encysted form is transmitted to a new host.

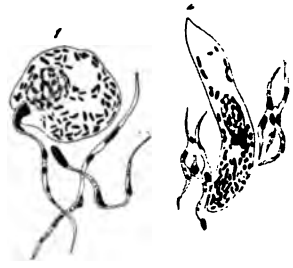


FIG. 24.—Sporogony of Plasmodium vivax Grassi and Feletti: zygosis. 1, Zygosis of one microgamete with the macrogamete; 2, oökinete and degenerate microgametes. (*After Schaudinn in Castellani and Chalmers.*)

Mechanism of Transmission.—The protozoan parasites of the blood (plasmodium, trypanosomes, etc.) are transmitted by the bite, of mosquitos, flies, ticks, etc. Those that have a direct development, as, for example, coccidia, ameba, etc., are usually transmitted in the encysted stage. The viruses of certain diseases, such as syphilis and trypanosomiasis, may invade the placenta, whereas others, as that of malaria, do not. The protozoan diseases are not transmitted by heredity, although in a few instances, as in *Babesia*, the germ may be carried in the egg of the tick to a new generation.

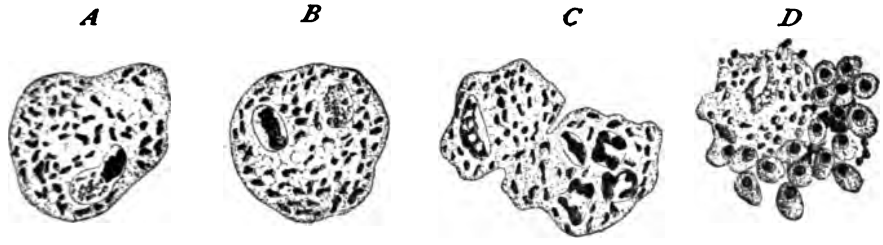


FIG. 25.—Regression and merozoite formation (parthenogenesis) in Plasmodium vivax. (*After Schaudinn.*) *A*, macrogametocyte in blood with nucleus differentiating into a denser and a lighter part; *B*, the denser part of the nucleus now divides preparatory to schizogony, *C*, *D*, while the paler portion with a part of the original cell degenerates; *D*, numerous merozoites formed about the divided nucleus. (*Calkins.*)

Pathogenesis.—Since it has become known that protozoa are the cause of important diseases of man and animals, much attention has been directed toward the study of these organisms. Among the diseases produced by the protozoa are: Sleeping sickness, caused by *Trypano-*

soma gambiense; dysentery, due to *Endamœba histolytica;* syphilis, caused by the *Treponema pallidum;* yaws, attributed to *Spirochæta pertenue,* and in particular malarial fever, which is now known to be due to one of the Plasmodia. This last-named condition is said to represent about one-third of all the diseases peculiar to tropical countries.

Classification.—The classic division of protozoa into Sarcodina, Flagellata, Sporozoa, and Infusoria, has in recent years been modified, owing to the fact that the life history of these organisms shows peculiarities that are common to two distinct groups. Because of this finding Schaudinn attempted to combine the Hemosporidia (Sporozoa) and the Flagellata into a single group; which he termed *Hemoflagellata.* Another cause for modifying the original classification was the discovery of new structures in the body of some of the protozoa; thus two varieties of nuclei were found to exist among the infusoria and the flagellata and others, such as the spirochetes and treponemas, previously included among the bacteria, were grouped with the protozoa. All this tends to show the difficulty that surrounds any attempt at satisfactory classification of the protozoa at the present time. The classification most generally accepted at the present time is the division of protozoa into—I. Plasmodromata (Döflein, 1903); II. Heterokaryota (Hickson, 1903).

I. *Plasmodromata.*—Under this head are grouped the protozoa that have well-defined nuclei, and in which the nuclear material is not differentiated into a macronucleus or trophonucleus, non-reproductive, and a reproductive or micronucleus portion. The Plasmodromata are divided into—

1. *Sarcodina.*—Plasmodromata that are mobile and take their nourishment by means of pseudopodia.
2. *Mastigophora.*—This class is characterized by the presence of flagella, which are used for locomotion and for the purpose of seizing food.
3. *Sporozoa.*—A variety characterized by its parasitic habit, complicated life history, and the absence of special organs of locomotion. Reproduction by sporulation is a distinctive characteristic of this group.

The Sporozoa are further subdivided according to Schaudinn into—(A) Telosporidia, and (B) Neosporidia.

A. *Telosporidia.*—A subdivision in which the reproductive phase or sporulation is distinct from and takes place after the trophic phase.

B. *Neosporidia.*—A class in which the reproduction phase or sporulation is not distinct from the trophic phase, but

takes place synchronously with the growth of the organism.

II. *Heterokaryota.*—These organisms, also called Ciliata, Infusoria, and Ciliophora (Döflein, 1903), are characterized by differentiation of the nuclear elements into a macronucleus or trophonucleus, and a micronucleus, or reproductive nucleus. These protozoa are provided with cilia either throughout their entire life or at some stage of development. They are divided into—(1) Ciliata and (2) Acinetaria.

1. *Ciliata.*—Cilia present throughout life.
2. *Acinetaria.*—Cilia present only during the early part of their life history.

CLASSIFICATION OF PROTOZOA

I. *Plasmodromata.* Nuclear elements not differentiated into a trophic (macronucleus) and a reproductive (micronucleus) portion.	1. *Sarcodina:*	Organism distinctly dysmorphic; presence of pseudopodia for locomotion and the taking of food; when parasitic, always extracellular.
	2. *Mastigophora:*	Presence of one or more flagella; when parasitic, usually extracellular.
	3. *Sporozoa.* Parasitic, usually intracellular; complicated life history. Absence of special organs for locomotion.	*Telosporidia:* Reproductive and trophic phases distinct; sporulation after completion of growth. *Neosporidia:* Reproductive and trophic phases not distinct; sporulation during growth.
II. *Heterokaryota.* Nuclear elements differentiated into a trophic (macronucleus) and a reproductive (micronucleus) portion; presence of cilia.	4. *Ciliata:*	Cilia present throughout life.
	5. *Acinetaria:*	Cilia present only in early life.

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CHAPTER IV

SARCODINA

Definition.—Morphology and Structure.—Habitat.—Motility.—Vitality—Artificial Culture.—Life History.—Mechanism of Transmission.—Pathogenesis.—Classification.—Endamebas of the Intestine: *Endameba coli; E. histolytica; E. tetragena; E. tropicalis; E. phagocytoides; E. undulans; E. braziliensis; Paramœba hominis.*—Endameba of the Mouth: *Endamœba gingivalis.*—Endameba of the Genito-urinary Tract: *Endamœba urogenitalis.* Pyogenic Endamebas: *Endameba pyogenes; E. kartulis; E. pulmonalis; Wahlkamphia tropicalis.*—Endamebas of the Viscera and Serous Cavities: *Endameba miurai; E. mortinatalium; Leydenia gemmipara.*—Erratic Endamebas.—Pseudo-endamebas.—Laboratory Search for Amebas.

Definition.—The Sarcodina or Rhizopoda are plasmodromatous protozoa that move about and seize their food by means of pseudopodia. They are found abundantly in nature as free living organisms, and also occur as parasites in man and the lower animals.

Morphology and Structure.—The Sarcodina are microscopic protozoa, variable in shape and size, and irregular in outline. They

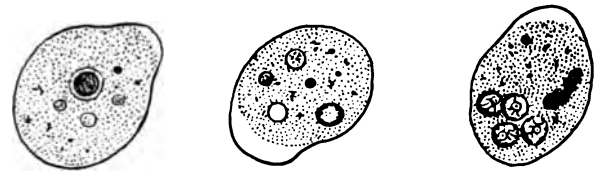


FIG. 26.—Diagram of 1, Endameba coli; 2, *E.* histolytica; 3, *E.* tetragena.

usually lack a distinct cell-wall, and this peculiarity permits the projection and retraction of pseudopodia. Structurally these organisms, like other protozoa, consist of a cytoplasm and a nucleus. The cytoplasm is more or less granular, and in some species is distinctly divided into an outer hyaline portion—the ectoplasm—and an inner granular portion—the endoplasm (Fig. 26). Food vacuoles are common, and occasionally contractile vacuoles are present.

The nucleus is usually conspicuous and rich in chromatin in the free amebas. It is also marked in some parasitic species, such as *E. coli*, but is much less distinct and hypochromatic in *E. histolytica* and other pathogenic varieties. In relation to the distribution and arrangement of the chromatin, three distinct types of nucleus in amebas have been described: (1) A *vesicular nucleus*, having a nuclear wall,

the chromatin being arranged at the periphery, with a clear space at the center; it is provided with one or several small chromatic grains, as in *E. histolytica;* (2) a *vacuolar nucleus,* which is clear with a distinct nucleolus and a scanty chromatin at the periphery, as in *E. Wahlkamphia tropicalis;* (3) a *hyperchromatic nucleus,* made up of a homogeneous chromatic body, as in *Parameba hominis* (Fig. 27).

Habitat.—Most of the parasitic rhizopodes in man are found in the large intestine, especially in the lower portion and in the rectum. Occasionally, however, they invade the internal organs, such as the liver (*E. histolytica*), kidney, lung, serous membranes, etc. The most favorable place for the development of amebas appears to be the mouth. Here they are very abundant, a fact that probably suggests that amebic infection of the intestine has its origin in the mouth. Amebas are not known to inhabit the circulatory system.

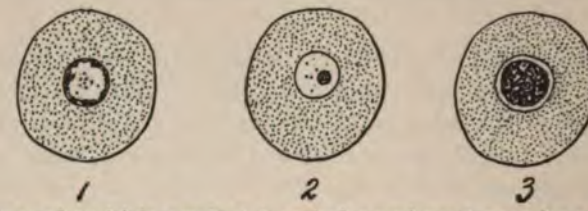


FIG. 27.—Types of nuclei in amebas; 1, vesicular nucleus; 2, vacuolar nucleus and 3, hyperchromatic nucleus.

Motility.—The amebas move by means of pseudopods, which are temporary organs of locomotion formed by the prolongation and retraction of the cytoplasm. In some species the movement is described as "rolling."

Vitality.—Amebas are very susceptible to the action of deleterious agents. In the non-encysted condition they are destroyed at 55° C. within a few minutes. The parasitic species of man becomes motionless at about 15° to 10° C., and a freezing temperature is fatal to them. They are destroyed by solutions of 1 : 200,000 to 1 : 100,000 emetin and 1 : 300,000 nitric acid; quinin also exerts a strong germicidal effect upon them. In the encysted condition they are more resistant and may withstand desiccation for months and the action of antiseptics for a considerable length of time.

Artificial Cultures.—Artificial cultures of parasitic amebas, such as *Endameba coli,* are easily obtained by symbiosis with bacteria (*B. typhosus, B. coli*). The requirements for growth are an appropriate medium, such as blood-agar or glycerin-blood-serum, a sufficient amount of moisture, and a temperature of 36° to 38° C. The material for cultivation is inoculated on a twenty-four-hour-old culture of *B. coli* or *B. typhosus,* and incubated at a temperature of about 36° C.

Transplantation of the culture to a new medium every day during the first week is recommended. This gradually eliminates the miscellaneous bacteria that were originally present, and also affords the amebas fresh material for growth. After a certain time—from one to three weeks—when the artificial growth has been established, encysted forms are found to be abundant, and the culture may be kept in this condition for a long time. Subsequent cultures may be made upon plain agar or upon any ordinary solid media. (For further details as to culture see Chapter XXIX.)

Life History.—The amebas reproduce asexually and sexually. Asexual reproduction takes place by binary fission, which begins by a direct or indirect division of the nucleus, followed by constriction and separation of the protoplasm into more or less equal halves. Reproduction by budding and gemmation, resembling spore formation, is believed to take place in *Endamœba histolytica*.

Sexual reproduction takes place by a process of autogamy. After developing asexually for some time, the organism becomes encysted, and the nucleus divides into two, each half undergoing maturation; the halves then conjugate and fuse again to form a *synkaryon*, which subsequently divides into two, four, eight, or more nuclei, each of which becomes surrounded by cytoplasm. Finally spores are formed, which, upon being set free, develop into young trophozoites (Fig. 17).

Mechanism of Transmission.—The amebas are transmitted to a second host in the encysted stage, and the infection usually takes place through contaminated food, water, uncooked vegetables, etc. On reaching the stomach and intestine, the cyst-wall is digested, the spores are set free, and amebas develop in the large intestine.

Pathogenesis.—*E. coli* is a parasite of the lower intestine, but apparently has no pathogenic properties. *E. histolytica* is the cause of tropical dysentery. This parasite not only causes ulceration of the colon, but it may also invade the liver and give rise to the formation of large abscesses. The pathogenic properties of certain amebas found in the lungs, kidneys, etc., are not definitely known. An ameba of the mouth, *E. buccalis* or *E. kartulis*, has recently come to be regarded as the cause of pyorrhœa alveolaris by Barrett, A. J. Smith, Bass, etc. It has not as yet, however, been definitely determined whether this protozoan is the cause or the effect of the disease.

Classification.—In accordance with their life habit and behavior, amebas have been divided into two classes—(1) Ameba and (2) Endameba. To Ameba belong all the free-living varieties. These are characterized by the presence of contractile vacuoles. To Endameba belong the parasitic species, which are characterized by the absence of contractile vacuoles.

Another system of classification divides the Rhizopoda into—(1)

Gymnoamœbida and (2) *Thecamœbida*. The former are characterized by a naked protoplasm; that is, the absence of a distinct cell-wall or shell. In this class are included most of the free and nearly all the parasitic species that occur in man. The Thecamœbida belong to the family *Gromidia*, and are characterized by the presence of a distinct and fixed cell-wall or shell. Only one species—*Chlamidophrys stercorea*—has been described as parasitic in man.

A third system of classification, based upon the appearance of the nucleus, is as follows: (1) *Endamebas*, characterized by the peripheral arrangement of the chromatin in the nucleus (vesicular nucleus) the nucleus is not distinct; (2) *Wahlkamphia*, characterized by the presence of a distinct nucleus, without peripheral chromatin in a rather large nuclear vacuole, and (3) *Paramebas*, in which the nucleus consists of a distinct chromatic body (Fig. 27).

For convenience of study the parasitic amebas of man will here be arranged according to the location they most commonly occupy in the body, as adopted by Brunyst, thus: 1. Endamebas of the intestine; II. Endameba of the mouth; III. Endameba of the genito-urinary tract; IV. pyogenic Endamebas; V. Endamebas of the viscera and serous cavities.

This arrangement has been followed solely for convenience, and is not a scientific classification; it is also subject to some exceptions. Thus, *E. buccalis*, although most commonly found in the mouth, may inhabit the large intestine; *E. pyogenes* may be found in any suppurating part of the body, and *E. histolytica* may be found in the liver-

I. ENDAMEBAS OF THE INTESTINE

1. **Endamœba (Lœschia) Coli** (Lösch, 1875). *Morphology.—Endameba coli* is normally found in the large intestine of man and animals. It is recognized by the absence of any sharp differentiation between the ectoplasm and the endoplasm, except when pseudopods are being formed. The ectoplasm is then seen to be a clear, hyaline zone at the end of the pseudopod. The parasite varies in length from 8 to 50 μ. The cytoplasm is finely granular, poor in food vacuoles, and contractile vacuoles are absent. In fresh preparations, the nucleus is distinctly seen as a refracting body, and when stained, the chromatin is seen to be arranged at the periphery, with one or several minute chromatic grains in the center. The location of the nucleus is subcentral.

In the encysted stage the ameba appears as a round body, about 25 μ in diameter, and provided with a somewhat thick membrane. It contains about eight nuclei.

Motility.—The *Endameba coli* is not actively motile, the pseudopods being slow in formation. More than two pseudopods are rarely visible at the same time.

Habitat.—Endameba coli is a common inhabitant of the large intestine of man and of many of the domesticated and wild animals (*e.g.*, mice, rats, guinea-pigs, monkeys, etc.). The parasites feed upon the contents of the bowel. The organisms seem to be more numerous when the reaction of the intestinal contents is normal. In cases of diarrhea or other intestinal disturbances the encysted forms are more apt to be present, especially if the reaction of the intestinal contents becomes slightly acid.

Life History.—Endameba coli is reproduced both asexually and sexually.

Asexual Reproduction.—This takes place either by binary fission or schizogony. In binary fission the nucleus divides amitotically and division of the cytoplasm subsequently occurs, the two young amebas thus formed separating and attaining adult size. Schizogony is a form of spore formation, and consists in the division of the nucleus into eight chromatin masses or nuclei, each becoming surrounded by protoplasm and developing into eight young spores (merozoites), which when set free, grow to be adult amebas.

Sexual Reproduction.—Sexual reproduction or sporogony in *Endameba coli*, as worked out by Casagrandi and Barbagallo and confirmed by Schaudinn, takes place by a process of autogamy. The order in which this occurs is as follows: (1) The parasite becomes encysted and leaves the host with the feces; (2) division of the nucleus into two daughter nuclei occurs, followed by division of the cytoplasm and the formation of two separate amebas; (3) chromatic fragmentation of the nuclei follows, with disappearance of a certain number of the chromatic granules (probably the vegetative elements) and rearrangement, in each half of the parasite, of the remaining chromidial grains (sexual element) into two new nuclei; thus two sexual cells, each containing male and female elements, are formed inside of the cyst-wall; (4) formation of three nuclei in each cell by subsequent division of the sexual nuclei takes place; (5) formation of two bisexual nuclei by absorption of two of the nuclei in each cell (probably the polar bodies) occurs; (6) there are division of bisexual nuclei and formation of two male and two female pronuclei; (7) formation of a synkaryon by cross-conjugation of the male pronucleus of one cell with the female pronucleus of the other, and vice versa takes place; (8) finally there is division of each synkaryon (or zygote) into two and each of these again into two nuclei, so that in all eight nuclei are formed, the whole becoming surrounded by a thick wall (Fig. 17).

Pathogenesis.—Endameba coli is a non-pathogenic commensal found in the intestine of man and in that of many of the lower animals.

Cultures.—Endameba coli, as previously stated, is easily cultivated artificially in symbiosis with other bacteria, upon various kinds of solid media. The requirements for growth are a proper degree of moisture, an appropriate medium—blood-agar or serum—and a temperature of 36° to 38° C. (See pages 62 and 63 and Chapter XXIX for further details.)

2. **Endameba (Lœschia) Histolytica** (Schaudinn, 1903). *Description.*—Endameba histolytica is from 20 to 50μ in length and differs from E. coli by the sharp differentiation of its cytoplasm into hyaline and granular cytoplasm (Figs. 26 and 28). The ectoplasm is best observed in the pseudopods, where it is seen to consist of a hyaline substance.

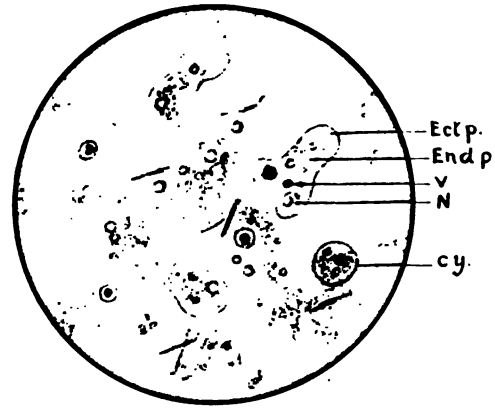


FIG. 28.—Endameba histolytica in the feces from a case of amebic dysentery in man. *Ectp*, ectoplasm; *Endp*, endoplasm; *V*, vacuoles; *N*, nucleus. One encysted form, *cy*, is also seen.

According to Schaudinn, the pseudopodia are capable of penetrating the mucous membrane of the intestine, and to this property the pathogenic activities of the parasite are ascribed. The endoplasm is more granular than in *Endameba coli*, and generally contains erythrocytes, bacteria, detritus, and numerous vacuoles. The nucleus is eccentric in location, and is less distinct and smaller than in *E. coli*. It is poor in chromatin and not readily stained. In the encysted stage the parasite is small, about 10–15μ. and contains four nuclei.

Motility.—Endameba hystolytica is actively motile, the pseudopods being rapidly formed and lobose in type. The movement of the parasite is described as rolling or flowing in character.

Habitat.—Endameba histolytica occurs as a parasite in the large intestine of man (Fig. 29), from which, under certain conditions, it escapes, to appear in abscesses of the liver, lung, brain, etc. (Fig. 30).

Recently the author found encysted amebas in preparations made from the discharge of pyorrhœa alveolaris. These cysts (Fig. 35)

measure from 10 to 15 in. in diameter, are thin walled and contain four nuclei resembling in all respects morphologically, the cysts of *Endameba histolytica* as found in the feces and ulcers of the intestine



FIG. 29.—Endameba histolytica in the mucosa of the rectum.

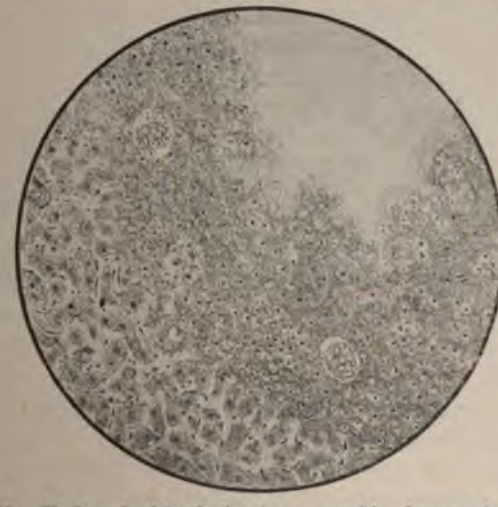


FIG. 30.—Endameba histolytica in an amebic abscess of the liver.

in cases of amebic dysentery. Vegetative and pre-encystment stages were also found in the same material.

The nature of this ameba is under study at present and if it should prove to be *Endameba histolytica*, this, to the author's knowl-

edge, is the first instance in which this parasite has been reported in the mouth in cases of pyorrhœa alveolaris.

The importance of this discovery will naturally open a fruitful field for investigation, namely: 1. The etiological relationship which pyorrhœa may have to amebic dysentery; 2. The possibility that *Endameba gingivalis* commonly found in pyorrhœa alveolaris may be identical to E. histolytica as suggested by Smith and Barret; 3. Whether such cases of pyorrhœa alveolaris are to a certain extent an external and local manifestation of amebic dysentery; 4. Whether in the life history of Endameba dysentery the pyorrhœa pockets act as reservoir or the point of entrance of the parasites where it undergoes a preliminary development and encystment preparatory to its successful en-

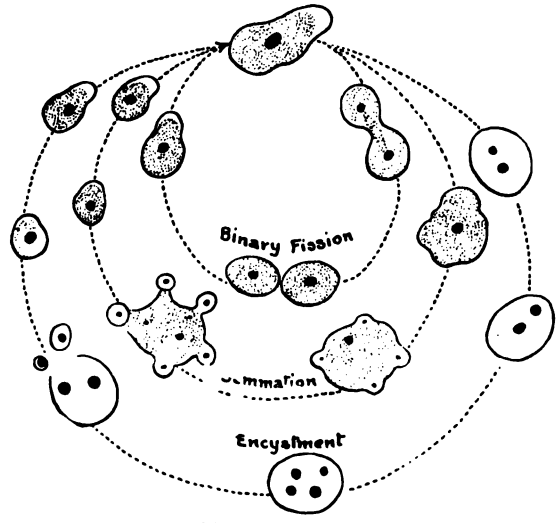


FIG. 31.—Life history of endameba histolytica.

trance and maintenance in the intestine of man; 5. Whether pyorrhœa alveolaris is an important predisposing factor to amebic dysentery.

Life History.—The works of Schaudinn, Lesage, and Noc have demonstrated only the asexual phase of reproduction of *Endameba histolytica*, which, according to these authors, may take place by binary fission, gemmation, or spore formation (schizogony). This spore formation, or encysted stage, is likely to occur in cases of chronic dysentery. When an encysted parasite is swallowed and reaches the intestine, the capsule is broken, and the young parasite is set free to grow into a typical ameba, after which the cycle is repeated.

Pathogenesis.—*Endameba histolytica* is the cause of amebic or tropical dysentery, liver abscesses, and abscesses in other parts of the body to which the parasite may happen to be carried by the lymphatic channels and eventually by the blood-stream.

Cultures.—The parasite has not been cultivated artificially. Lesage claims to have cultivated the parasite *in vitro* by using peritoneal exudation, and Noc described the cultivation of an endameba resembling *Endameba histolytica* in symbiosis with bacteria.

3. **Endameba (Lœschia) Tetragena** (Viereck, 1904). *Description.*—In this organism the cytoplasm is differentiated into ectoplasm and endoplasm. This parasite bears a resemblance to *E. coli* in that it is said to undergo encystment and sexual reproduction. According to Bensen, the presence of chromidial masses in the cytoplasm is a characteristic

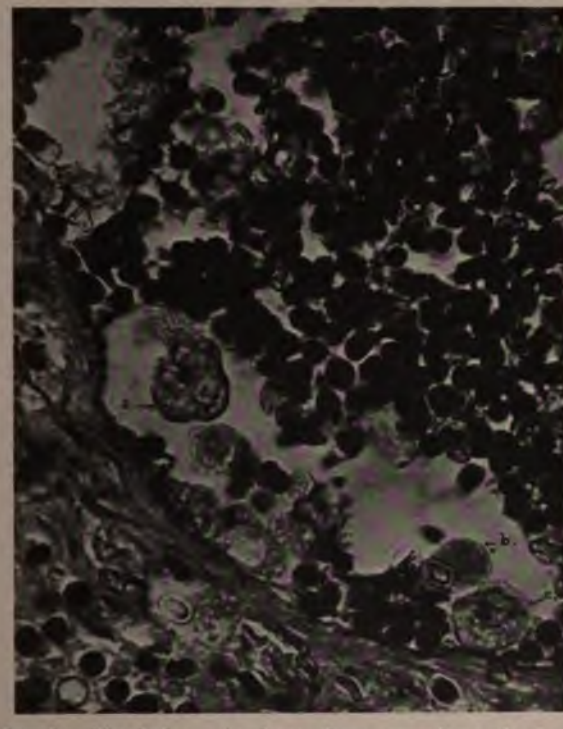


FIG. 32.—Endameba histolytica. At least three organisms (*a*, *b*, and *c*) within lumen of thrombosed vein under base of dysenteric ulcer.

feature of this organism. The nucleus is relatively large and distinct, and contains central chromatin granules or centrioles.

Habitat.—*Endameba tetragena* has been found by Viereck and Hartman in the intestine of man in cases of dysentery.

Life History.—Reproduction takes place asexually and sexually. The asexual reproduction takes place by binary fission, and consists in amitotic division of the nucleus, followed by division of the cytoplasm.

The sexual reproduction is accomplished by autogamy, as in

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or zygote) a single synkaryon
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ng regarded as the cause of certain
but in recent years the parasites
significance, and at present it is
cause of tropical dysentery than to
the two parasites may be identical.

STICS OF ENDAMŒBA COLI;
ND E. TETRAGENA

	E. Coli.	E. Tetragena.
	10 to 70μ. Differentiated from the cytoplasm.	About 10 to 40μ. Same as *E. histolytica*.
	Thin, excellent, more refractile. No chromatoid bodies mentioned, presence of erythrocytes.	Similar to *E. histolytica* plus characteristic chromatoid bodies.
	Rapid in formative and actively motile.	Similar to *E. histolytica*.
	Very active.	Similar to *E. histolytica*.
	Numerous, indistinct, poor in chromatin.	Similar to *E. histolytica* plus presence of vacuole.
	Similar to man.	Same as *E. histolytica*.
	Normal.	Same as *E. Coli*(?).
	Very small (7–15μ), contain four nuclei.	Same as *E. histolytica*, contain four nuclei.
	Cause of tropical dysentery.	Same as *E. histolytica*.

Tropicalis (Lesage, 1908).—This organism, believed to be a harmless parasite. It was
man in the tropics. It resembles *E. coli* and
with it, although, according to Lesage, it is dif-
by the small size of its cysts and the presence
as well as by the fact that its cytoplasm is
ndoplasm and endoplasm.

Phagocytoides (Gaudcheau, 1908).—This
China in the intestine in a case of dysentery.
organism, measuring 12 to 15μ in length, its
about that of a leukocyte. Its cytoplasm

is differentiated into ectoplasm and endoplasm, and spirochete-like bodies have been seen in it. The parasite can be cultivated in artificial media in symbiosis with *B. typhosus* or other bacteria, and is probably similar to *E. coli*.

6. **Endameba (Lœschia) Undulans** (Castellani, 1905).—This endameba was found in the intestine in case of diarrhea in association with Cercomonas, Trichomonas, and other protozoa, and probably represents a developmental stage of *Cercomonas hominis* (Castellani). The organism is from 10 to 30μ in length, the cytoplasm being differentiated into ectoplasm and endoplasm. It is finely granular, and is occasionally provided with a non-contractile vacuole. Its chief characteristics are the presence of an undulating membrane without flagella and the rapid formation and retraction of a single long and slender pseudopodium.

7. **Endameba (Lœschia) Braziliensis** (de Beaurepaire Aragao, 1912).—This organism resembles *E. coli* in its vegetative form. It is characterized by the presence, in the encysted stage, of an equatorial streak, which stains black with iron hematoxylin (siderophilic substance).

8. **Parameba (Craigia) Hominis** (Craig, 1907).—This parasite was found by Craig in the Philippine Islands in cases of severe diarrhea. It is from 15 to 30μ in length. The ectoplasm is differentiated from the endoplasm; the nucleus is composed almost entirely of chromatin, and in the encysted stage it contains several nuclei or spores that, when set free, become flagellated bodies (Craig).

II. ENDAMEBA OF THE MOUTH

1. **Endameba (Lœschia) Gingivalis** (Gross, 1849).—*Endameba gingivalis*, called also *E. buccalis* (Prowazek, 1904) and *Ameba dentalis* (Grassi, 1877), is a common parasite of the mouth. It is found under almost any conditions, although it is most abundant in caries and in cases of suppuration, such as occurs in pyorrhea alveolaris. M. T. Barrett and A. J. Smith, Bass and Johns and others regard this parasite as the cause of pyorrhea. The organisms vary in size from 6 to 32μ; the cytoplasm is well differentiated into ectoplasm and endoplasm; the nucleus is distinct, but poor in chromatin. Reproduction takes place by binary fission and by encystment, and probably also by spore formation.

As to other amebas found in the mouth and described by several investigators, mention may be made of *A. buccalis* (Steinberg 1862), *A. dentalis* (Grassi 1879), *E. kartulis* (Döflein 1904), *A. maxilaris* (Kartulis), *E. buccalis* (Prowazek), etc. These amebas probably are identical to *Endameba gingivalis*.

Oral Endamebiasis and Pyorrhœa Alveolaris.—So much comment has arisen in recent years regarding the etiological significance of these

amebas to pyorrhœa alveolaris, that a brief remark on this disputed question may here be considered.

The knowledge that amebas are found in the mouth is a generation old, but their rôle in the affection, pyorrhœa alveolaris, has been the subject in recent years of much investigation.



FIG. 33.—Endameba gingivalis. (*Gross.*) Reproduced from Dental Cosmos, Sept., 1914. (*After A. J. Smith.*)

Chavarro regarded the amebas as favorable agents, by acting as scavengers in destroying bacteria and small protozoa commonly found in the pyorrhœa pockets; contrary to this, by not a few investigators, this parasite is believed to be the cause of the affection.

That these protozoa when present are the source of further morbid changes and destruction of the gums admits of no doubt, but that they are the primary cause of pyorrhœa alveolaris cannot be admitted without due reservation, as actual proof of it is still lacking.



FIG. 34.—Endameba gingivalis. (*Gross*). Unstained material from pyorrhœa pocket. *N*, nucleus.

The problem is still more complicated if we take into consideration that pyorrhœa alveolaris is a mixed infection in which great numbers of bacteria and other protozoa than amebas are found, such as Spirochetes, Trichomonas, etc., which are often associated; moreover not uncommonly amebas are not found in the discharge from the pockets.

We believe that the consensus of opinion at present is that pyorrhœa alveolaris is not necessarily due to amebas, but that it represents a mixed infection induced by several organisms. It is probable that the occurrence of amebas is rather the effect than the cause of the affection, but this does not imply that these parasites are harmless as they represent a complication which like all secondary infections, not only aggravate the condition, but also may predispose to other local and constitutional disturbances.

Another point which may be raised in this connection is the fact

that endamebiasis of the mouth may be considered as an indication that such patients either because of their habit of life, diatetic conditions and gastro-intestinal derangement in association with constitutional disturbances and environmental conditions are more susceptible to infection in general and particularly to allied affections such as intestinal endamebiasis.

An interesting point in this conncetion also is our recent finding of vegetative and encysted ameba in the pockets of pyorrhœa (Fig. 35) which morphologically are identical to *Endameba histolytica*. It is common knowledge that dysentery is often associated with pyorrhœa

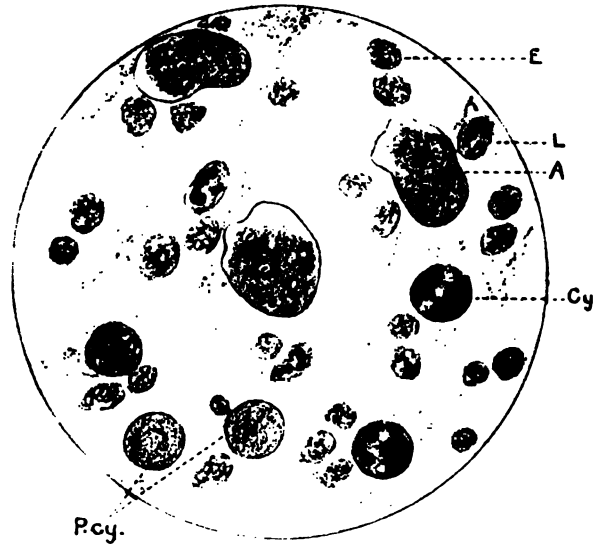


FIG. 35.—Vegetative and encysted forms of ameba (*Endameba histolytica*) in proportion from the discharge of pyorrhea alveolaris. *E*, Erythrocytes; *L*, Leukocytes; *A*, ameba; *Cy.*, cyst; *P.cy.*, precystic stage.

alveolaris and although this may be a coincidence on account of the fact that pyorrhœa is a more common affection, nevertheless the saparozoitic or semi-parasitic habit of the amebas in the mouth, living as they do in these pyorrhœa pockets, differs in no essential point from the habitat of *E. histolytica* in similar pockets in the ulcers of the intestines.

Both amebas, therefore, requiring similar environmental conditions for their existence, they must of necessity have similar predisposing conditions in their mode of infection and consequently pyorrhœa alveolaris if it does not represent the primary or local manifestation of dysentery, at least may be regarded as an important predisposing factor of the disease. The above brief discussion concerning the etiology of pyor-

rhœa alveolaris and its relation to amebic dysentery may be summarized as follows:

1. The amebas found in the pockets of pyorrhœa alveolaris are not the cause but rather the effect of the infection.
2. This amebic infestment represents a complication or secondary infection which undoubtedly aggravates the condition.
3. Amebas resembling Endameba histolytica are found in the pockets of pyorrhœa alveolaris.
4. *Endameba gingivalis* probably is identical to *E. histolytica*, the minor morphological variations between the two being due to environment.
5. Pyorrhœa alveolaris is an important predisposing factor to amebic dysentery and probably in not a few cases it represents a local and the primary manifestation of the disease in which Endameba histolytica undergoes development and encystment preparatory to its successful entrance and lodgment in the intestines.

III. ENDAMEBA OF THE GENITO-URINARY TRACT

Endameba (Lœschia) Urogenitalis (Baelz, 1883).—This parasite, which is also called *E. vaginalis* (Blanchard, 1885), has been found by several observers (Baelz, Posner, Kartulis, Jürgens, and others) in cases of metritis, vaginitis, cystitis, and other affections of the genito-urinary organs, but its etiologic bearing in these diseases is not definitely known. Morphologically, it resembles *E. coli*, and its presence in the genital tract is probably accidental.

IV. PYOGENIC ENDAMEBAS

1. **Endameba (Lœschia) Pyogenes** (Verdun and Bruyant 1911).—This organism was found by Verdun and Bruyant in the purulent discharge of an abscess of the lower jaw. It measures 20 to 35μ in length in the vegetative form, and 8 to 15μ when encysted. The encysted form is provided with from one to four nuclei, and in this respect resembles, *E. tetragena* with which it probably is identical.

2. **Endameba (Lœschia) Kartulis** (Döflein, 1901).—This organism was found by Kartulis in Egypt, and by Flexner in Baltimore, in an abscess of the lower jaw. It is probably identical with *E. pyogenes.*

3. **Endameba (Lœschia) Pulmonalis** (Artault, 1898).—This endameba was found by Artault in cavities of the lung, free in the pus, but not in the walls of the abscesses. Morphologically it resembles *E. buccalis*, with which it probably is identical. Its presence in the lung is apparently accidental.

4. **Wahlkamphia Tropicalis** (Lesage, 1908).—The wahlkamphia are characterized by the absence of peripheral chromatin in the nucleus and the presence of a distinct nucleolus. The parasite is usually a free-living organism, and is not uncommonly provided with from one to three flagella. One species, *W. tropicalis*, has been observed by Whitmore, Chaton, Gauducheau, and others in the pus of hepatic abscesses.

V. ENDAMEBAS OF THE VISCERA AND SEROUS CAVITIES

1. **Endameba (Lœschia) Miurai** (Ijima, 1898).—This organism was found by Miura in the pleura and in the peritoneal exudate in a case of cancer. Similar ameboid bodies have been found by Lauenstein, Behla, and others in the ascitic fluid of carcinoma cases, but their etiologic significance has not been determined.

2. **Endameba (Lœschia) Mortinatalium** (A. J. Smith and F. D. Weidman, 1910).—This ameba was found by Smith and Weidman in the fixed stained tissues of the kidney, lungs, and liver of a still-born syphilitic child. The organism is described as oval, oblong, pyriform or irregular in shape, measuring 0.025 to 0.032 mm. in diameter. The ectoplasm is poorly differentiated from the endoplasm; the nucleus is relatively large, spheric or oval, and contains a nucleolus.

3. **Leydenia Gemmipara** (Schaudinn, 1896).—This organism was detected by Lieberkühn and Leyden in the ascitic fluid collected from persons suffering from malignant growths. According to Schaudinn, it is spheric or irregular in shape, and measures 3 to 36μ in diameter. The ectoplasm is differentiated from the endoplasm; and the nucleus is large and vesicular. Schaudinn regards it as the ameboid stage of *Chlamydophrys enchelys*.

Genus Chlamydophrys (Cienkowsky, 1876).—These organisms resemble the ameba, but are inclosed in shells and provided with openings through which numerous fine pseudopods are extruded. They belong to the family *Gromidiæ*, which are free-living organisms. One species, *C. stercorea*, has been found parasitic in man.

Chlamydophrys stercorea (Cienkowsky, 1876).—This organism has also been called *C. echelys*, and is frequently found in the feces of cows, rabbits, mice, and lizards. Schaudinn found it in the ascitic fluid from cases of carcinoma.

Erratic Endamebas and Pseudo-endamebas.—The foregoing list includes most of the pathogenic endamebas that at some time, and under certain conditions, have been found in man. Other endamebas have been found in abscess cavities, in ulcers, in tumors, and in the normal cavities of the body (mouth, ears, etc.), under morbid conditions, but these were probably present accidentally, and have

no bearing on the origin of the disease. The occurrence of endamebas in parts of the body remote from their normal habitat, or the accidental presence of saprozoic types in connection with morbid conditions, has sometimes led to the common species being regarded as new parasitic varieties. This is probably the case with *E. coli* and *E. tropicalis* (Lesage); *E. tropicalis* and *E. hominis* (Walker); *E. buccalis* and *E. dentalis; E. kartulis* and *E. buccalis* or *E. histolytica* (Döflein); *Chlamydophrys enchelys* and *Leydenia gemmipara*. If to these we add the list of other supposedly ameboid bodies that have been found in the preserved tissues of tumors, etc., and that are probably merely degenerated cells or embryonic cells in the stage of regeneration or degeneration (plasma cells, fibroblasts, polyblasts, etc.), or macrophages that, because of their ameboid shape, vacuolation of the cytoplasm, etc., have been mistaken for amebas, we can readily see that the list may be greatly increased.

Laboratory Search for Amebas.—The material to be examined—feces, pus, exudate, etc.—should be collected in clean vials, free from germicidal chemicals, and especially prepared for the purpose. The examination should be made as soon as possible after the material has been collected, for these organisms survive only a few hours outside the host. If, for any reason, this cannot be done, the material should be kept moist and at about the body temperature, when the amebas will remain alive and fairly active for several hours. The examinations of fresh cover-glass preparations is more satisfactory than that of fixed and stained specimens. The film preparations should be as thin as possible, a carefully cleaned slide and cover-glass being used. It is well to examine first with a low power of the microscope and with the diaphragm almost entirely closed. The amebas appear as refractive objects, attached to the slide or cover-glass; they are irregular in outline and vary in shape. The organisms are easily recognized by their irregular outline, refractive character, and by the fact that while other particles of the specimen may be flowing with the currents of the fluid, the amebas usually do not change their position, but remain at a certain point in the field of the microscope. A subsequent examination of any suspected object may be made under the dry high power of the microscope. The identification of amebas should be based upon their motility and pseudopod formation, but encysted forms can also be easily recognized.

At times the motility appears to be very slow, especially in winter, when the temperature of the room may be low. In this case the slide may be warmed over the flame of a Bunsen burner until it reaches a temperature of about 36° or 40° C., when more rapid movement of the organisms takes place.

The encysted stage is easily recognized by the highly refractive

character of its substance. The cyst of *E. coli* measures 20–30μ; that of *E. histolytica* is much smaller, and measures 7–15μ; the cysts of *Lamblia* are very much smaller.

In preparing permanent mounts the smears are fixed, while moist, in a saturated alcoholic solution of mercury bichlorid, which is later removed with Lugol's solution, which in turn must be washed away with alcohol. Hematoxylin and eosin, Giemsa's and methylene-blue are suitable stains.

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CHAPTER V

FLAGELLATA

Definition.—Morphology and Structure: The Cytoplasm; the Vacuoles; the Undulating Membrane; the Chromatic Substance; the Trophonucleus; the Kinetonucleus; the Flagellum.—Motility.—Polarity of Flagellates.—Habitat.—Nutrition.—Reproduction; Multiplication in the Proboscis; Multiplication in the Alimentary Canal.—Pathogenesis.—Classification.

Definition.—The Flagellata or Mastigophora are plasmodromatous protozoa, usually of a fixed and distinct shape, and provided with one or more flagella that serve for locomotion, as a sensory organ, and in some instances for obtaining food.

Morphology and Structure.—Generally speaking, the *Mastigophora* are characterized by a distinct and fixed shape (usually elongated, spindle, or globular). Schaudinn includes *Spirocheta* and *Treponema*, previously regarded as bacteria, among the flagellates. In the simplest forms, *Spirocheta* and *Treponema*, the organism is a slender, spiral body, provided either with a fine flagellum at one or at both ends, or a delicate, undulating membrane, as the case may be. In the higher forms, with the exception of *Rhizomastigina* and others that are ameboid, the bodies of flagellates are elongate or spindle shaped, and in the most specialized types, such as the *Trypanosoma*, the parasites are usually spindle shaped and differentiated into cytoplasm, nuclear substance, undulating membrane, and a flagellum (Fig. 36).

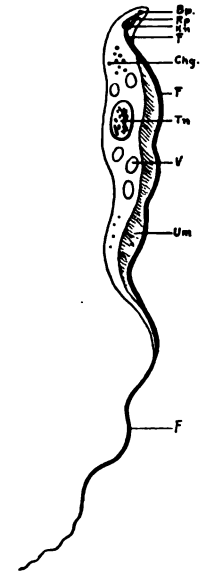


FIG. 36.—Diagram of a trypanosome. *Bp*, blepharoplast; *Rp*, rhizoplast; *Kn*, kinetonucleus; *F.*, flagellum; *Tn*, trophonucleus; *Um*, undulating membrane.

The Cytoplasm.—In *Spirocheta* and *Treponema* the cytoplasm is scanty. The organisms, like bacteria, consist chiefly of chromatic substance in the form of chromidial grains scattered through the scanty protoplasm all over the body of the organism. Among the higher types (*Mastigota*), the cytoplasm consists of ectoplasm and endoplasm, whereas in *Trypanosoma* it is specialized into *periplasm*, which enters into the formation of the undulating membrane and the sheath of the flagellum, and *endoplasm*, the latter containing the vacuoles and nuclei.

The Vacuoles.—The vacuoles seen in *Trypanosoma* are usually three in number, and appear as clear spaces about the middle of the body. They are food vacuoles, and are best seen under dark-field illumination.

The Undulating Membrane.—This is a part of the periplasm. It runs along one side of the body of the parasite, with which it may end, though it may project beyond, to form part of the flagellum. The line followed by the membrane is regarded as the dorsal surface of the parasite, and in its course it may be fortified by myoneme threads. The base of the membrane is in the cytoplasm, and its free edge is continuous with the cytoplasmic portion of the flagellum, to which it is attached, forming the sheath of the flagellum.

The Chromatic Substance.—In the lower forms, *Spirocheta* and *Treponema*, the chromatic or nuclear substance of the organism is distributed throughout the body in the form of chromidial grains. The body of the organism is made up chiefly of these chromatic particles, embedded in a scanty cytoplasm. The term *diffused nucleus* is commonly applied to this type of nuclear substance.

In the higher forms, such as *Trypanosoma*, the chromatic substance is divided into two distinct bodies or masses of unequal size—the *trophonucleus* and the *kinetonucleus*.

The trophonucleus, also erroneously called *macronucleus*, has a purely nutritive function. It is relatively large, distinct, and situated at about the middle of the body or slightly toward the flagellated end. The structure of the trophonucleus is not definitely understood—by some it is regarded as vesicular, having chromosomes inside and a chromatic sphere or centrosome in the center. The trophonucleus of *Trypanosoma lewisi* is said to contain eight chromosomes. It appears as an oval mass, which is differentiated into a peripheral chromatic zone with chromatic granules in the center.

The kinetonucleus, also misnamed *micronucleus* or *blepharoplast*, is situated at the non-flagellated end of the parasite. It is exceedingly small, rich in chromatin, and stains deeply. The blepharoplast is usually found within the kinetonucleus, but in more highly differentiated forms, it is situated outside of the kinetonucleus. It is from this body that the flagellum arises. Occasionally, however, the blepharoplast, which is in reality a centrosome, may be absent or invisible and in such cases the kinetonucleus serves as blepharoplast, and hence the name blepharoplast has also been applied to the kinetonucleus.

Between the trophonucleus and the kinetonucleus, when properly stained, there may be seen an aggregation of deeply stained, minute bodies, called *chromatoid granules*. These are at times aggregated into small masses, which have the appearance of a rudimentary micronucleus.

The chromatic substance of a typical flagellate, such as *Trypanosoma*, is therefore, differentiated into a trophonucleus, which is concerned with nutrition, a kinetonucleus, which is chiefly concerned with motion, and an achromatic body, the blepharoplast or centrosome, which appears as a small bead giving origin to the flagellum.

The Flagellum.—A typical flagellum consists of an elastic axial core, more or less completely inclosed in a cytoplasmic sheath. It runs outward through the endoplasm to the ectoplasm, where it gives rise to the undulating membrane; it next turns and runs along the remaining part of the body, in which it may end, or it may project beyond the body as a free, whip-like process. A flagellum is made up of three portions: the *root*, in the *endoplasm;* the *undulating portion*, in the *ectoplasm;* and the *free portion*, or *end-piece*. In certain species or in the developmental stages, the flagellum may project directly from the endoplasm and ectoplasm to the external surface of the parasite, as in Herpetomonas or Crithidia.

If the blepharoplast is absent, the flagellum arises directly from the kinetonucleus, or, more properly, from the centrosome or *centrosome blepharoplast* inside of it. The centrosomes may be single or multiple, depending on the number of flagella. When a blepharoplast is present and is located outside of the kinetonucleus, a strand of achromatic substance, the *rhizoplast,* runs between the two; this may be considered either as an outgrowth from the blepharoplast or as the central spindle (centrodesmose) of the achromatic elements of the dividing nucleus connecting the divided portion of the original centrosome. The parts of the flagellum as they originate, therefore, are the blephoroplasmic, rhizoplasmic, kinetic, endoplasmic, and periplasmic, and the end-piece or free end.

The position and number of flagella have formed a basis of classification of the flagellates; thus if the flagellum is situated anteriorly, it is called *tractellum;* if posteriorly, *pulsellum;* the group in which only one flagellum is present is termed *monomastigota;* that in which two or more flagella of equal length are present, *isomastigota;* if these are of unequal length, the group is called *paramastigota;* if several flagella are present these are termed *polymastigota;* and if the flagella are numerous and scattered over the body, they are placed in the group *holomastigota*.

Motility.—The chief functions of the flagellum are generally believed to be locomotion and the obtaining of nutriment. This is undoubtedly the case with certain free-living forms, such as *Euglena*, for example, and also with certain evolutional forms, such as *Crithidia* and *Herpetomonas*, in which the flagellum is given off directly from the body of the parasite and the undulating membrane is absent or rudimentary. In a typical trypanosome, however, in which the

undulating membrane is well developed, the latter appears to be of greater importance than the flagellum in effecting locomotion. In primitive types of flagellates, *e.g.*, *Spirocheta* and *Treponema*, the organisms move in a circular and spiral direction, accompanied in *Spirocheta*, by a serpentine bending of the body; as they are provided with a flagellum at each end, they can move in either direction. It would seem, therefore, that the flagellum, by acting as a tactile organ, serves also as a means of orientation. In the higher forms, such as *Crithidia*, *Herpetomonas*, *Euglena*, *etc.*, the movement is usually in one direction, the flagellum being directed forward. Trypanosomes act similarly, but because of the presence of an undulating membrane, they may move in either direction. As a rule, however, they progress with the flagellum directed forward.

Polarity of Flagellates.—A diversity of opinion exists as to which is the anterior and which the posterior end of a flagellate. Sambon, Castellani, Chalmers, and others believe that the non-flagellated end of the blood parasites (trypanosomes) represents the anterior end of the organism, since in its course through the red blood-cells that part goes first. Others, however, hold the opposite view. As a matter of fact, a careful examination, under a dark-field illuminator or under the ordinary microscope, of a very thin layer of the fresh blood of a rat infected with *Trypanosoma lewisi*, shows the parasites to be capable of moving in both directions, although movement with the flagellum forward is the more common. The writer has sometimes observed trypanosomes at rest that showed only slight vibratory movements of the undulating membranes, but more marked oscillatory movements of the flagella, and has also noticed occasional rotary movements, such as are seen in *Euglena*. This finding would suggest that the flagellum may be a tactile organ as well as one of locomotion, and resembling an antenna in function. This being the case, may not the flagella be regarded as corresponding to the anterior end of the organism?

Habitat.—Parasitic flagellates are usually found in the blood of the host, although certain forms, such as *Treponema*, and *Trypanosoma*, sometimes display a tendency to infiltrate the tissue or to become localized in certain organs.

Nutrition.—Food is absorbed from the liquids in which the parasites live by osmosis.

Reproduction.—Among *Spirocheta* direct longitudinal division is generally recognized. In *Trypanosoma* both sexual and asexual reproduction has been observed.

Asexual reproduction usually takes place in the blood of the host, although it may also occur in artificial culture. Two types are recognized—binary fission and roset formation (Fig. 37).

According to Prowazek and Byloff, binary fission in trypanosomes is accomplished after a complex nuclear division, but Moore, Breinl, and Hindle have shown that this may take place with or without growth. Multiplication is brought about first by amitotic division of the kinetonucleus and trophonucleus, followed by the formation of a new flagellum in the daughter parasite, division of the cytoplasm, and separation of the two individuals. Such division has been observed in *T. lewisi* and *T. gambiense* (Plate I).

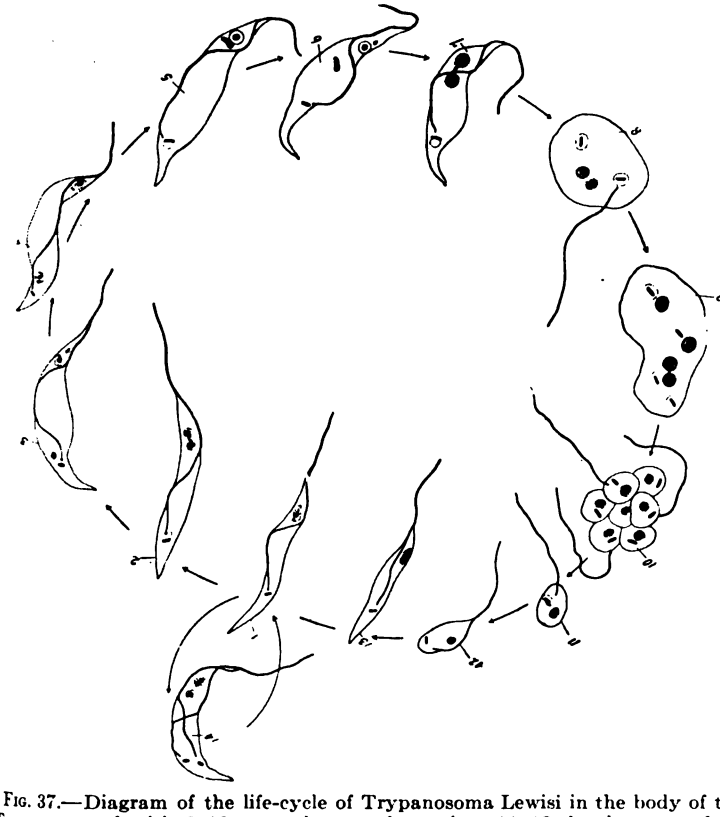


FIG. 37.—Diagram of the life-cycle of Trypanosoma Lewisi in the body of the rat. 1, Trypanosoma lewisi; 2–10, stages in roset formation; 11–13, development of a small flagellate form into a trypanosome; 14, binary fission. (Constructed from drawings by Moore, Breinl, and Hindle in the *Annals of Tropical Medicine and Parasitology*. (*After Castellani and Chalmers.*)

According to the same observers, roset formation takes place as follows: (1) Amitotic reduction of the trophonucleus and the kinetonucleus, the latter giving off a body that travels to the trophonucleus. In *T. gambiense*, in place of this body a strand is formed between the trophonucleus and the kinetonucleus; (2) division of the trophonucleus and the kinetonucleus and the formation of fission masses consisting of two, four, or more small young parasites in the stage of

formation, provided with the single old flagellum; (3) formation of several flagella in the fission mass, and differentiation of this mass into distinct young organisms; (4) finally, the cycle is completed by the separation of the young parasites into distinct organisms, which become free and attain adolescence.

Very little is known regarding the *sexual reproduction* in trypanosomes. Theoretically the existence of differentiated sexual forms—male and female—in the blood of the vertebrate is assumed, and it is believed that these conjugate and, when taken into the body of the invertebrate host, a blood-sucking insect, as is the case in *Plasmodium malariæ*, undergo further development. These views have not as yet been confirmed by actual observation. Prowazek recognizes three forms in *Trypanosoma lewisi;* (1) male; (2) female, and (3) indifferent forms. According to Holms, however, only two forms are seen—males and females.

The male forms are described as being very slender and actively motile, and as having long flagella and elongated and deeply staining nuclei.

The female forms are broad, are sluggish in motion, and have short flagella, a reticulated cytoplasm, and a round nucleus that is poor in chromatin.

In the indifferent forms, which are the most common, the cytoplasm is granular and the nucleus is imperfectly defined and possessed of poor staining properties.

Nevertheless it must be admitted that so many intermediate forms occur that the three types mentioned are not sharply defined, and may merely represent different stages of growth and development.

The conjugation between the male and female forms of *Trypanosoma* has been but rarely observed, and in the few instances on record (those of Keysselitz and Prowazek) it is doubtful whether they were not merely examples of ordinary division. From our present knowledge of the subject we learn that asexual reproduction of *Trypanosoma* may take place in the invertebrate host, either in the proboscis, the alimentary canal, the salivary glands, or the eggs.

Multiplication in the Proboscis.—The method in which multiplication of *Trypanosoma gambiense* and *T. brucei* in the proboscis of *Glossina palpalis* takes place is described by Roubaud as follows: (1) disappearance of the undulating membrane; (2) shortening of the flagellum; (3) approach of the kinetonucleus to the trophonucleus; (4) attachment of the parasite to the proboscis, and finally (5) multiplication with formation of masses of parasites. The entire process consumes but a few minutes.

Multiplication in the Alimentary Canal.—In the case of *Trypanosoma granulosus*, a trypanosome of fresh-water fish, multiplication

may take place in the anterior part of the alimentary tract—the crop of the leech *Hemiclepsis marginata*. It consists in a simple binary fissure, formation of Crithidial forms, and their final development into slender trypanosomes that eventually migrate to the proboscis (Brumpt). In other trypanosomes, such as *T. rajæ*, multiplication takes place in the body of the leech *Pontobdella maricata*, and consists in the formation of Leishmania-like bodies which, on passing to the intestine, develop into Crithidial forms with the final formation of long and slender trypanosomes that migrate to the proboscis. *These slender forms represent the infective stage in the life history of the parasite.*

The Infective Stage in the Salivary Glands.—According to Bruce, the proboscis of *Glossina palpalis* is not involved in the further development of *T. gambiense*. In from five to seven days after feeding the trypanosomes disappear, and the insect becomes infective only after three or four weeks. During this time the parasites multiply in the lumen of the intestines, probably at first intracellularly and later extracellularly. From the intestine they migrate to the salivary gland by way of the proboscis and salivary duct as short, stumpy forms, which represent the infective stage.

Rectal Encystment and Ovum Infection.—This mode of development and infection has not been definitely known to occur.

Pathogenesis.—The flagellates are etiologic factors in a number of serious diseases of man, as, for example, syphilis (*Treponema pallidum*), yaws (*T. pertenue*), relapsing fever (*S. recurrentis*), *Kala-Azar* L. (*Leishmania donovanni*), sleeping sickness (*T. gambiense*), American trypanosomiasis (*T. cruzi*), and certain mild affections of the external genitalia (*Trichomonas vaginalis*) and of the intestine (*Lamblia intestinalis*).

Classification.—Owing to the present state of our knowledge concerning the flagellates, no satisfactory classification of the group can be made. The methods most in use at the present time are those of Döflein and Hartman. The chief point of difference between the two methods consists in classifying the blood flagellates, which are grouped by Döflein under the head of *Protomonadina*, whereas Hartman placed them under a new order, *Binucleata* which are characterized by the presence of a trophonucleus and a kinetonucleus. Döflein's classification is as follows:

MASTIGOPHORA:
- *Subclass Flagellata* (Euflagellata):
  - Order I. *Protomonadina.*
  - Order II. *Polymastigina.*
  - Order III. *Euglenoidina.*
  - Order IV. *Chromomonadina.*
  - Order V. *Phytomonadina.*

Subclass Dinoflagellata.
Subclass Cytoflagellata.

Under the head of *Protomonadina* are included the *Trypanosomidæ* and allied families, *i.e.*, the *Hemoflagellata*. Under the *Telosporidia*, a subclass of the *Sporozoa*, are included the *Plasmodidæ*, *Hemoproteidæ*, *Leukocytozoidæ*, and allied forms, such as the *Hemosporidiæ*. The *Spirocheta* and *Proflagellata* are treated separately.

Hartman's classification is as follows:

Subclass Flagellata:
Order I. *Rhizomastigina.*
Order II. *Protomonadina.*
Order III. *Binucleata.*
Order IV. *Chromomonadina.*
Order V. *Euglenoidina.*
Order VI. *Phytomonadina.*

The *Protomonadina* and *Polymastigina* of Döflein are grouped under the order *Protomonadina*, which is divided as follows:

Order II. Protomonadina:
(A) *Monozoa* (not bilaterally symmetric).
Family 1. *Cercomonadidæ.*
Family 2. *Bodonidæ.*
Family 3. *Monadidæ.*
Family 4. *Tetramitidæ*, etc.
(B) *Diplozoa* (bilaterally symmetric).
Family: *Distomatidæ.*

The classification adopted in the second edition of Castellani and Chalmers is as follows:

Phylun Mastigophora Diesing, 1866.
Class I. Euflagellata, Cohn amended Bütschli.
Order 1. *Protomonadina*, Blochmann.
Order 2. *Polymastinina*, Blochmann.
Order 3. *Binucleata*, Hartman.
Order 4. *Euglenoidinæ*, Blochmann.
Order 5. *Chromomonadina*, Klebs.
Order 6. *Phytomonadina*, Blochmann.
Class II. Dinoflagellata, Bütschli.
Class III. Cystoflagellata Haeckel.

Among the *Protomonadina*, *Polymastigina*, and *Binucleata* are included the parasitic species found in man. The following are the differential characteristics of these three orders:

ORDER I. *Protomonadina.*—These flagellates are provided with one or three flagella and the undulating membrane is absent. Some are free and others are parasitic. The free forms are frequently provided with a collar or cystostoma (*Choanoflagellidæ*, Stein), but have no esophagus. The parasitic forms (*Cercomonadiæ*, Kent) are elongate or short, not uncommonly oval in shape, and provided with one or several flagella, a contractile vacuole at the flagellated end, and have an ameboid, non-flagellated extremity. The most important species that are parasitic to man are *Cercomonas hominis* (Davaine, 1854) and *C. vaginalis* (Castellani and Chalmers, 1909).

ORDER 2. *Polymastigina.*—These flagellates are provided with from two to eight flagella, and with a special cystostoma or oral aperture for the reception of food. The undulating membrane may be either absent, as in *Heteromita ceylanica*, or present, as in *Trichomonas*. They are free or parasitic in habit. *Trichomonas hominis*, *T. vaginalis; T. dysenteriæ*, *T. pulmonalis*, and *Lamblia intestinalis* are the parasitic species found in man.

ORDER 3. *Binucleata.*—These are usually parasitic flagellates of the blood of vertebrates. They are found either free in the serum or inclosed in the cellular elements of the blood. They are characterized by having a trophonucleus and a kinetonucleus. Reproduction takes place asexually (schizogony) and sexually (sporogony), the latter being brought about by the conjugation of similar or dissimilar gametocytes.

The common trypanosome is an example of the order *Binucleata*, but since Schaudinn's researches on the life cycle of a *Hemoproteus noctua* and *Leukocytozoa danielewskyi*, it has been shown that the genus *Halteridium*, belonging to the *Hemosporidia*, is merely a stage in the life history of a flagellate. The researches of Hartman and Raven on *Proteosoma* showed the relation that exists between the *Hemosporidia* and *Hemoflagellata*, which have been included by these authors among the *Binucleata*, an order that embraces five families: (1) *Hemoproteidæ;* (2) *Leukocytozoidæ;* (3) *Trypanosomidæ; Herpetomonidæ;* (5) *Plasmodidæ*, and possibly a sixth family, the *Spirochætidæ*, a possibility that is based on the assumption that *Spirochæta* would eventually be found to be allied to the *Binucleata*.

Sambon divides the Binucleata into two sections: *Acystina* and *Encystina* and five families. The former are *Binucleata* in which the oökinete does not become encysted, but remains free, and the latter are *Binucleata* in which the oökinete becomes encysted. The family *Plasmodidæ* is probably the only one in which a typical encystment of the oökinete takes place.

MASTIGOPHORA: Order III. *Binucleata*, Hartman.
Section I. Acystina, oökinete free.

Family 1. *Hemoproteidæ.*
Family 2. *Leukocytozoidæ.*
Section II. Encystina, oökinete encysted.
Family 3. *Trypanosomidæ.*
Family 4. *Herpetomonidæ.*
Family 5. *Plasmodidæ.*

As has previously been stated, these classifications are far from satisfactory, and will probably be modified in the near future. For convenience we will follow the division of parasitic flagellates found in man into *Spirochetidæ, Trypanosomidæ, Cercomonidæ,* and *Lambliaidæ* as adopted by Brumpt with some modification. The *Plasmodidæ* will be described under the hemosporidian *Sporozoa.*

CLASSIFICATION OF PARASITIC FLAGELLATES OF MAN

Family	Characteristics	Genus	Species
I. Spirochetidæ	Body not rigid, filiform and spiral in shape; number of spirals variable. Undulating membrane present; flagellum absent or inconspicuous; nuclear substance diffused in the body in the form of chromidia grains.	Spirocheta	*S. recurrentis* *S. duttoni* *S. carteri* *S. novyi* *S. berbera* *S. vincenti* *S. buccalis*
	Body rigid, spiral in shape, number of spirals constant and equidistant from one another. One single flagellum at each end; undulating membrane absent or not seen; nuclear substance diffused through the body in the form of chromidia grains.	Treponema	*T. pallidum* *T. pertenue*
II. Trypanosomidæ	Body spindle in shape; binucleated (trophonucleus and kinetonucleus); flagellum single and well developed; undulating membrane prominent. Usually extracellular parasites.	Trypansoma	*T. gambiense* *T. rhodesiense* *T. cruzi*
	Body oval or round in shape; binucleated; flagellum rudimentary or absent; no undulating membrane. Usually endocellular parasites.	Leishmania	*L. donovani* *L. furunculosa* *L. infantum* *L. nilotica* *L. braziliense*
	Body elongated; binucleated; flagellum single and well developed; undulating membrane rudimentary or absent.	Crithidia	*C. braziliense*
III. Cercomonidæ	Presence of three or four flagella; undulating membrane distinct.	Trichomonas	*T. vaginalis* *T. intestinalis*
	Body pyriform; presence of one or several flagella; undulating membrane absent or rudimentary.	Cercomonas	*C. longicauda*
	Body irregular and ameboid; presence of two flagella.	Prowazekia	*P. asiatica* *P. cruzi* *P. weinbergi*
	Presence of cystostoma with three flagella; no undulating membrane.	Tetramitus	*T. mesnili*
IV. Lambliaidæ	Body pyriform; presence of cystostoma and eight flagella; no undulting membrane.	Lamblia	*L. intestinalis*

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CHAPTER VI

FLAGELLATA (Continued)

THE PARASITIC FLAGELLATES OF MAN

I. Family *Spirochetidæ*.—II. Family *Trypanosomidæ*.—III. Family *Cercomonidæ*.—IV. Family *Lambliaidæ*.

I. FAMILY SPIROCHETIDÆ (Ehrenberg, 1883)

History—Morphology and Structure—Life Cycle—Mechanism of Transmission—Artificial Cultures—Pathogenesis—Classification.

The spirochetes are flexible, thread-like organisms, cork-screw spiral in shape, and measuring from 8 to 16μ in length, as in *S. recurrentis*, to 150μ in *S. balbianni*. They closely resemble the *Binucleata*, and particularly the trypanosomes, in certain features, and bacteria in others. Previous to the work of Schaudinn, in 1904, they were regarded as bacteria, but of late there has been a tendency among biologists to classify them among the flagellated protozoa. These organisms are the etiologic factors in certain diseases, such as relapsing fever, syphilis and yaws.

History.—The first pathogenic spirochete was discovered by Obermeier in 1868 in human blood, and was studied by Metchnikoff and Soudakiewitch. In 1904 Dutton and Todd demonstrated the transmission of African fever by the tick (*Ornithodorus*). Schaudinn, in 1904, discovered the *Treponema pallidum*, which has been shown to be the cause of syphilis, and Castellani, in 1905, isolated the *Treponema pertenue*, which is the cause of yaws.

Morphology and Structure.—The body of a spirochete is made up of endoplasm and periplasm, the latter entering into the formation of an undulating membrane or a terminal flagellum, as the case may be. The endoplasm is granular, and contains a diffuse nucleus, which consists of achromatic filaments with bars of chromatin (chromidial grains). In addition dots of chromatin—the basal granules—are present at one or at both ends.

Life Cycle.—Reproduction may take place by either longitudinal or transverse division, the former method being by far the more common. According to Fanthom and Porter, in *S. recurrentis* and *S. balbianii* this mode of reproduction is manifested first by division of the basal granule, followed by division of the membrane and cytoplasm. The separation into male and female elements and the

encystment and conjugation described by some authors are regarded as doubtful, although it is possible that conjugation and sporogeny in *S. duttoni* may take place in the tick (Fig. 38).

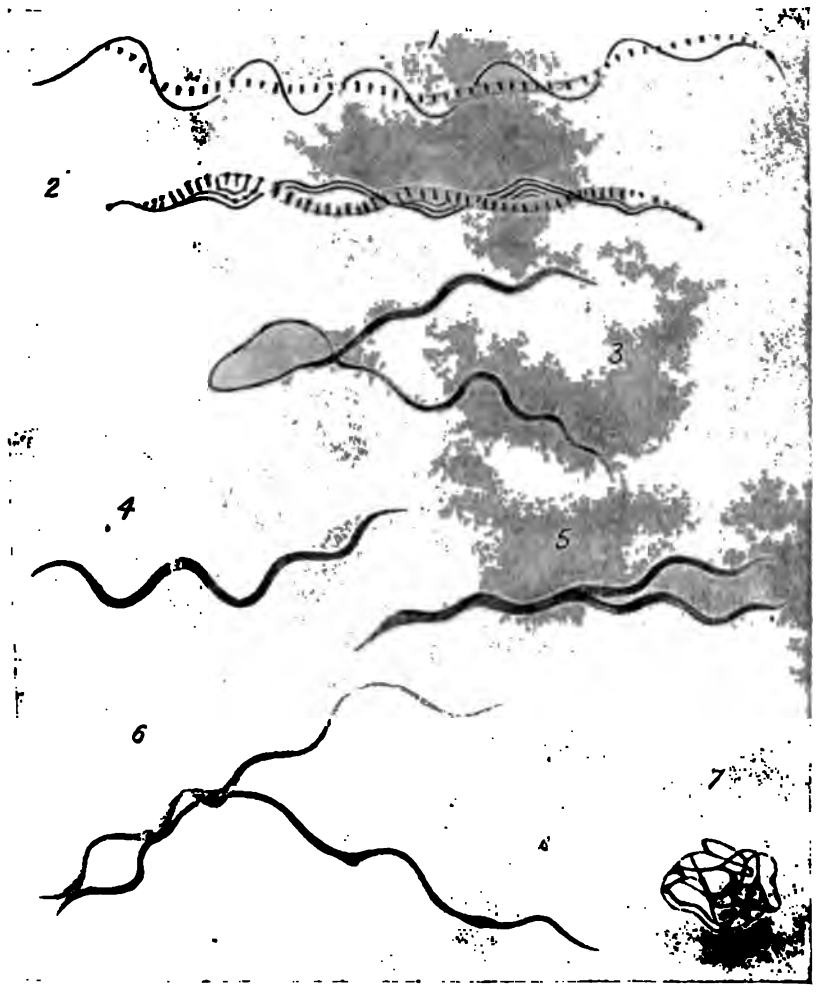


FIG. 38.—Spirochætes. 1, Spirochæta anodontæ, showing the undulating membrane and chromatic bars. (*After Fantham, Quarterly Journal of Microscopical Science.*) 2, Spirochæta balbianii, showing fibrillæ in undulating membrane. (*After Fantham.*) 3–7, Spirochæta *duttoni*. (*After Breinl, Annals of Tropical Medicine and Parasitology.*) 4, shows the uncolored transverse band; 5, longitudinal division; 6, possible male and female forms; 7, encystment. (*After Castellani and Chalmers.*)

Mechanism of Transmission.—In some species, as in *S. recurrentis*, the parasite is transmitted through the bite of an intermediate host—an arthropod. Others, such as *Treponema pallidum* and *T. pertenue*, are transmitted directly by contact.

Artificial Cultures.—Successful artificial cultivation of *Treponema pallidum* has been accomplished by Noguchi and others, but all attempts to cultivate the spirochetes have not as yet been successful.

Pathogenesis.—The most important and most familiar of the species pathogenic for man are *S. recurrentis*, which is the cause of relapsing fever, *Treponema pallidum*, the etiologic factor in syphilis, and *T. pertenue*, the cause of yaws.

Classification.—The family *Spirochetidæ* is divided into two genera: (1) *Spirocheta* and (2) *Treponema*. The former are characterized by the presence of an undulating membrane and the absence of flagella or tapering ends, and the latter by the presence of flagella and the absence of an undulating membrane. These distinguishing characteristics are not, however, always clear; thus, although the undulating membrane is plainly evident in *S. balbianii*, in *S. recurrentis*, it is almost imperceptible, and although the flagellum is seen on spreads stained preparations of *Treponema pallidum*, it is but rarely observed in the tissue preparations stained by Levaditi's silver impregnation method.

GENUS SPIROCHETA (Spirochaudinnia)

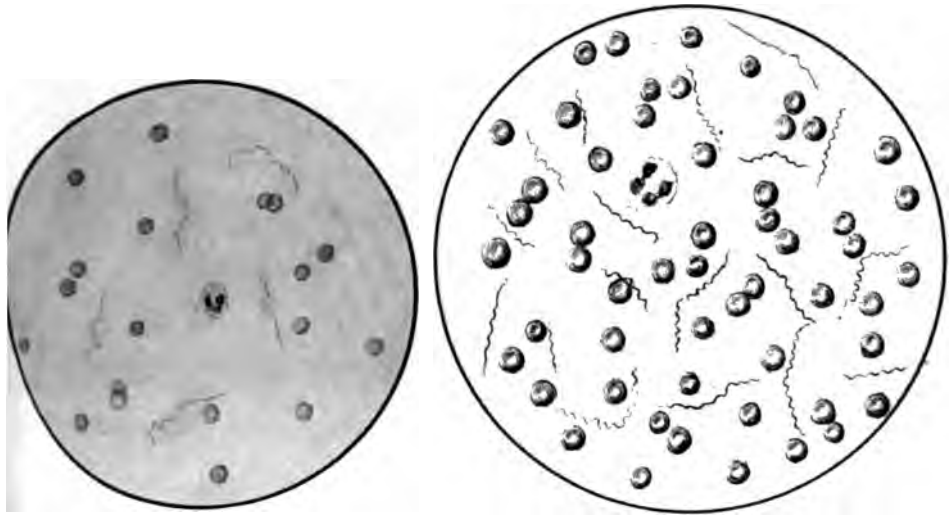
The most important variety of the pathogenic spirocheta is *S. recurrentis*. It is a blood parasite, and has been proved to be the cause of relapsing fever. This disease is characterized by a pyrexia that continues for from three to six days and is followed by a period of quiescence or intermission during which the temperature returns to the normal. On about the fourteenth day, as a rule, a relapse occurs. This is usually more severe than the primary febrile attack, but lasts only three or four days, and generally terminates in recovery by crisis.

Obermeier, in 1868, first found the parasite in the blood of a case of relapsing fever, and it became known as the *Spirillum obermeieri*. Later the organism, being recognized as a spirochete, was named *S. recurrentis*. Still later it was found that other species existed, and *S. duttoni*, *S. novyi*, *S. carteri*, etc., were isolated, each organism being the cause of a slightly different variety of relapsing fever. Morphologically, the species are identical, but some are pathogenic for laboratory animals whereas others are pathogenic only for monkeys. The differentiation is made chiefly by observing the phenomenon of agglutination with immune sera. If an animal is immunized against *S. recurrentis*, its serum is capable of agglutinating only this organism, and it will have no agglutinating effect upon *S. berbera*, *S. novyi*, or *S. carteri*, except in great concentration.

1. **Spirocheta recurrentis.** (Lebert, 1874). (*Spirillum obermeieri*, Cohn, 1877).—*Spirocheta recurrentis* is a blood parasite and

the cause of relapsing fever. It is found in the blood during a febrile attack of the disease.

Morphology.—The organism is relatively small, extremely slender, very flexible, and spiral in shape. It is from 8 to 9μ in length and about 0.25μ in width. Elongated developmental and agglutination forms, from 16 to 19μ or even 100μ in length, may sometimes be found in hyperimmune blood, toward the end of the disease, or in the interval between relapses. The structure of the organism has not been described in detail. In the short forms a single flagellum has been observed by Novy and Knapp, but its presence has been denied by Nuttall.



A *B*

FIG. 39.—Spirochæta recurrentis. *A*, in human blood; *B*, in rat blood experimentally infected.

Habitat.—The parasite is found in the blood and internal organs, especially during the primary attack and with each relapse. During the interval between attacks the parasites are so few in number as not usually to be found in the peripheral blood. The organism also lives in the bedbug, which may act as a passive host for the transmission of the parasite.

Animal Inoculation.—*S. recurrentis* is pathogenic for monkeys, rats, and mice, in which animals it produces a marked infection that ends fatally in from three to eight days, according to the amount injected (Fig. 39).

Life History.—No life history of *S. recurrentis* has been described. The parasite has been found to remain alive for some days in certain blood-sucking insects, such as bedbugs, fleas, etc., and it is probable that these may serve as intermediate hosts.

Mode of Infection.—Manteufel and others have succeeded in infecting rats and mice by the application of parasitized blood to the skin. Brumpt has observed *S. duttoni* in the menstrual fluid of monkeys. It is possible that the infection of man by *S. recurrentis* takes place by contact, through an abrasion of the skin, but the tendency of the time is to attribute the condition to fleas, bedbugs, and lice, and to refer the transmission of the parasites to the bites of these insects, though this fact has never be demonstrated.

Pathogenesis.—*S. recurrentis* is the cause of European relapsing fever.

2. **Spirocheta duttoni.** (Novy and Knapp, 1906).—*Spirocheta duttoni*, also called *Spirillum duttoni*, like *S. recurrentis*, is a blood parasite and the cause of relapsing fever in Africa—commonly known as *African tick fever.*

Morphology.—The parasite is somewhat larger than *S. recurrentis*, being from 16 to 20μ long by 0.2μ in width. The number of spirals varies from two to ten, the distance between them being about 2.2μ.

Structurally the parasite consists of a periplast and a central core or endoplasm. According to Dutton and Todd, the periplast contains an undulating membrane, a statement that is denied by Breinl. The central core or endoplasm consists of a darker or chromatic substance, and a lighter or achromatic portion. During convalescence the chromatic portion is believed to break up into granules and, coincidentally, the parasites disappear from the blood.

Habitat.—The parasite is found in the peripheral blood and free in the plasma serum, especially during the febrile attack and during subsequent relapses; it is also present, but in smaller number, during the interval between attacks. According to Breinl, just before the crisis the organism may be found in the spleen, bone-marrow, and liver. Not uncommonly it may be observed either phagocytized or in the encysted form inside of a leukocyte or other cell, in which it breaks up into small granules from which new generations are believed to develop. The parasite may also live and multiply in the tick, whith therefore acts not only as a passive but also as an active host. The disease is transmitted to man by the bite of the tick.

Animal Inoculation.—*Spirocheta duttoni* is inoculable into dogs, goats, sheep, rabbits, guinea-pigs, rats, and mice. Cats, chickens, pigeons, and gold fish are immune. For inoculation purposes the infected blood is drawn into a citrate salt solution, or it may be defibrinated and injected into a susceptible animal—either directly into the circulation, into the, peritoneal cavity or into the subcutaneous tissue.

Life History.—*S. duttoni* requires an intermediate host—the tick—for its complete development and transmission. Two phases of

reproduction are, therefore, described for the parasite—one in the vertebrate and the other in the invertebrate host. In the vertebrate host, man, for example, *S. duttoni* passes through two stages—one extracellular, in the plasma of the blood, and the other intracellular. In the free or extracellular stage the parasite reproduces chiefly by longitudinal division, and, according to certain authors, also by transverse division. The intracellular reproduction that takes place in the cells of the internal organs is accomplished by a process of encystment that somewhat resembles spore formation. The parasite enters a cell, winds itself into a small coil, and becomes encysted. In this condition it gradually becomes less and less distinct, and by a process of schizogony—probably by fragmentation—the chromatic substance breaks up into very minute, ultramicroscopic granules, each of which is believed to be capable of growing into a new spirochete. These minute granules are so small as to pass through a Pasteur-Chamberland filter, and this would account for the filtrability of the virus discovered by some authors.

The cycle of development of *S. duttoni* in the invertebrate, according to Leishmann, takes place in the tick, *Ornithodoros moubata*. When the tick bites and infected person, the parasites, on entering the intestinal tract of the tick, lose their motility and extracellular and intracellular reproduction takes place in a manner somewhat similar to the multiplication in the vertebrate host, previously described, except that in the lumen of the intestine the parasites, before undergoing division, may be seen in the form of stout, slender, and very long organisms. Intracellular reproduction takes place in the cells of the intestine and in the Malpighian tubules. Here the chromatin divides into fine or coarse granules, with the possible formation of comma-shaped bodies that eventually grow into young spirochetes.

According to Leishmann, the extracellular cycle of *S. duttoni*, which takes place in the lumen of the intestine of the tick, manifests itself by fragmentation of the chromatin into minute bodies of bacillary or coccoid shape; these multiply and pass into the cells of the intestine and Malpighian bodies, and, on being discharged with the feces, or regurgitated with the contents of the alimentary canal, are inoculated into another host, while feeding, by means of the proboscis. On reaching the circulation these bodies develop into young spirochetes, and the cycle is repeated. From the Malpighian tubules these bodies may pass into the ovary and infect the developing eggs, the infection being thus transmitted to a new generation of ticks (Dutton and Todd). It is also believed that the tick may remain infective to the third generation (Maller).

Mechanism of Infection.—*S. duttoni* is transmitted to a new host through the bite of an infected tick. This does not take place by

means of the saliva, but is carried in by the small bodies in the contents of the alimentary canal. The tick is believed to remain infective for over one year (Maller). The infection may also probably take place directly through an abrasion or wound of the skin or mucous membrane, or by contact with parasitized blood.

Pathogenesis.—The *Spirocheta duttoni* is the cause of African relapsing fever, also known as African tick fever. This disease closely resembles European relapsing fever, but is less severe, of shorter duration, and relapses are frequently absent.

3. **Spirocheta Carteri** (Mackie, 1907).—This organism is the causative factor in the relapsing fever of India.

Morphology.—The parasite is long and slender, being from 10 to 30μ in length and about 0.2 to 0.5μ in width. It displays a tendency to form long chains of several individuals, which may attain a length of from 80 to 90μ.

Habitat.—*S. carteri* is a parasite of the blood of man.

Animal Inoculation.—Experimentally the parasite can be transmitted to monkeys, rabbits, guinea-pigs, rats, and mice. The organisms can live for some days in bedbugs. It lives also in lice and possibly in mosquitoes.

Life Cycle.—*S. carteri*, like other spirochetes multiplies chiefly by longitudinal division. The fact that it can live for days in the body of an arthropod suggests the possibility of some developmental cycle in them.

Mechanism of Infection.—Mackie demonstrated the transmission of the parasite into monkeys through the bite of an infected bedbug (*Cimex rotundatus*), and it is possible that this may also be the route of transmission of the disease to man.

Pathogenesis.—*S. carteri* is known to be the cause of the relapsing fever of India, a grave disease with a mortality rate that is said to reach 38 per cent.

4. **Spirocheta Novyi** (Schellach, 1907).—*Spirocheta novyi* is a slightly longer parasite than *S. recurrentis*, *i.e.*, from 19 to 29μ in length. It is the cause of American relapsing fever, a disease that resembles closely the European form.

Habitat.—The organism inhabits the blood, where it is found in large numbers during the febrile attack.

Animal Inoculation.—The parasite is inoculable into rats and mice.

Life History.—*S. novyi*, contrary to what is generally observed in most spirochetes, multiplies chiefly by transverse division.

Mechanism of Infection.—The virus may be transmitted to man directly through abrasions in the epidermis, but it is probable that some blood-sucking arthropod is responsible for its transmission.

5. **Spirocheta Berbera** (Sergent and Foley, 1910).—Morphologically, *S. berbera* is identical with *S. recurrentis.* It is from 12 to 18μ in length by 0.2 to 0.3μ in width, and exhibits from four to eight spiral twists.

Habitat.—The organism is a blood parasite of man, but may live also in the bodies of fleas.

Animal Inoculation.—The parasite may be transmitted from man to monkeys, but not from monkey to monkey. Successful inoculation of rats is difficult, and can be accomplished only by injecting large doses into young animals.

Life History.—The reproduction of *S. berbera* probably takes place chiefly by longitudinal division.



FIG. 40.—Spirochæta vincenti, other spirochætes and an ameba in pus from pyorrhea alveolaris.

Mechanism of Infection.—Transmission of the parasite to man is probably effected directly through abrasions or wounds in the skin or mucous membrane. Indirect infection through the medium of an intermediate arthropod host has not been demonstrated.

Pathogenesis.—*S. berbera* is regarded as the cause of a distinct type of relapsing fever occurring in the north of Africa (Algiers, Tunis, and Tripoli).

6. **Spirocheta vincenti** (Blanchard, 1906).—This parasite may sometimes be found in the mouth under normal conditions, but is far more frequently seen in cases of suppuration, such as pyorrhea alveolaris, abscesses, and other inflammatory or necrotic conditions of the oral cavity and in Vincent's angina. The organism is from 12 to 25μ in length. It is differentiated from other spirochetes by the relatively small number of undulations in the body (Fig. 40).

Habitat.—The parasite is commonly associated with *Bacillus fusiformis* and with amebas in the mouth. It is fairly constant in cases of pyorrhea alveolaris and other suppurative oral processes, and occurs also in necrotic and ulcerative conditions of the skin.

Pathogenesis.—*S. vincenti* is regarded as the cause of Vincent's angina (angina ulceromembranosa), hospital gangrene, noma, and ulcus tropicum. Sufficient evidence, however, has not been adduced to show that the organism is the etiologic factor in such cases; for it may be present merely as a saprozoite.

7. **Spirocheta buccalis** (Cohn, 1875).—This organism is a normal inhabitant of the mouth, and is found almost constantly in the saliva and in the tartar of the teeth. It is from 15 to 20μ in length and resembles *S. vincenti*, with which it may be identical. No pathogenic properties have been attributed to it.

8. **Spirocheta Morsus Muris.**—This flagellate found by Futaki, Takaki and Osumi in the skin in cases of "rat-bite fever" is regarded by these authors as the cause of this disease. The microörganisms are intermediate in size between *Treponema pallidum* and *Spirochæta recurrentis*, the coils are variable in shape and number. It has not been demonstrated in the saliva of infected rats.

9. **Spirocheta (Leptospira) Icterohemorrhagica: Sp. Nodosa.**—This is the flagellate found by Inada and Ido in 1915 in the blood in cases of "Infectious Jaundice or Weil's Disease" in Japan. The microörganism is also found in the cerebrospinal fluid, urine and tissues of the body especially during the thirteenth to the fifteenth days of the disease after which they gradually disappear. Japanese investigators have shown the rat to act as the reservoir of the virus. In coal mine districts in Japan, where the disease occurs, as many as 40 per cent. of the rats were found infected.

The microörganism is variable in size, measuring from 5 to 20μ in length, the coils are not preformed and variable in shape and number. Not uncommonly one end of the parasite presents a hook-like appearance which is characteristic.

10. **Leptospira Icteroides.**—This microörganism recently found by Noguchi in the blood and tissue of yellow fever patients in Guayaquil is regarded by this author as the cause of the disease.

Noguchi describes the parasite as a delicate filament finely wound at short and regular intervals, slightly thicker at the middle and gradually tapering at both ends. It measures 4 to 9μ in length and 0.2μ in width. It is unrecognizable under the ordinary microscope but can be seen under the darkfield illumination as a beaded-like motile filament. When stained by Giemsa or Wright, after fixation with osmic acid, it appears somewhat thicker and the coils are less in num-

ber and irregular, not uncommonly presenting a hook-like bending at one or both ends.

The parasite can be cultivated aërobically and is inoculable into young dogs six to seven weeks old and specially into guinea pigs. Donkey, horse, sheep, pigs and cats and birds in general are refractory to the infection.

The virus pass through the pores of Berkefeld filter *V* and *N* which suggest the possibility of a granular phase of the microörganism. The exact relation which this flagellate bears to Leptospira sclerohemorrhagica and the production of yellow fever when inoculated into man has not been as yet determined.

Other spirochetes that should be mentioned are:

S. dentium (Miller), which inhabits the human mouth.

S. refringens (Schaudinn), occurring in ulcerations about the genitalia and in association with *Treponema pallidum* in syphilitic chancre.

S. acuminata (Castellani), occurring in the ulcerative lesions of yaws.

S. obtusa (Castellani), which is present in the ulcerative lesions of yaws.

S. microgirata (Gaylord and Calkins).

S. aboriginalis—Cleland found this organism in a case of granuloma inguinalis.

S. schaudinni (Prowazek), believed to be the cause of ulcus tropicum. It is probably transmitted by the leech.

S. bronchialis (Castellani), found in the sputum in cases of bronchitis.

S. pyogenes (Mezinescus), found in purulent discharges.

Spirochetes not yet determined have been discovered in dysentery (Le Dante), in the bone-marrow in a severe case of anemia (Moritz), etc.

GENUS TREPONEMA (Schaudinn, 1905)

These parasites are minute, thread-like organisms, whose rigid bodies are twisted into numerous corkscrew-like curves. They are characterized by the presence of fine tapering ends that form flagellum-like appendages, and by an absence of undulating membranes. These characteristics serve to differentiate them from the spirochetes, to which they are closely allied. The genus consists of three species, which two, *T. pallidum* and *T. pertenue*, are of special interest.

Treponema pallidum (Schaudinn, 1905).—Treponema pallidum is a delicate, spiral organism, from 6 to 14μ in length and 0.2 to 0.5μ in width, found in the lesions of syphilis. The body of the parasite, like that of other treponema, is rigid; the spirals, from six to twelve

in number, are preformed and equidistant from one another. The periplast of one or both ends of the organism tapers to a delicate prolongation, seen only in stained preparations, and is regarded as a flagellum. There is no undulating membrane (Fig. 41).

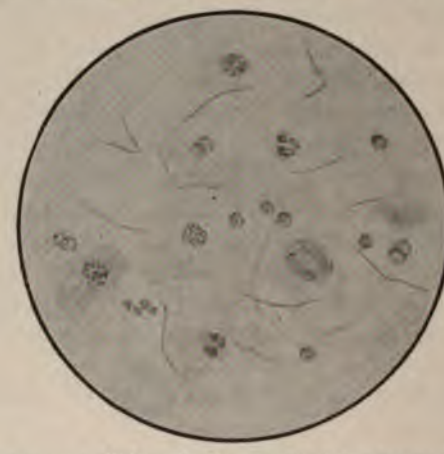


FIG. 41.—Treponema pallidum in the purulent discharge from a chancre.

Motility.—In preparations made from a syphilitic chancre the organism is seen, under dark-field illumination, to move by a rotatory motion around the long axis, either forward or backward.



FIG. 42.—Treponema pallidum in the lumen of blood-vessel, glomeruli, uriniferous tubules and interstitial tissue of the kidney from a case of congenital syphilis.

Habitat.—*T. pallidum* is a parasite of man, and is found in the lesions of syphilis. It occurs in great numbers in the primary lesion of the disease, known as the chancre. In the secondary lesion it can be found only after prolonged search, and in the tertiary lesion it

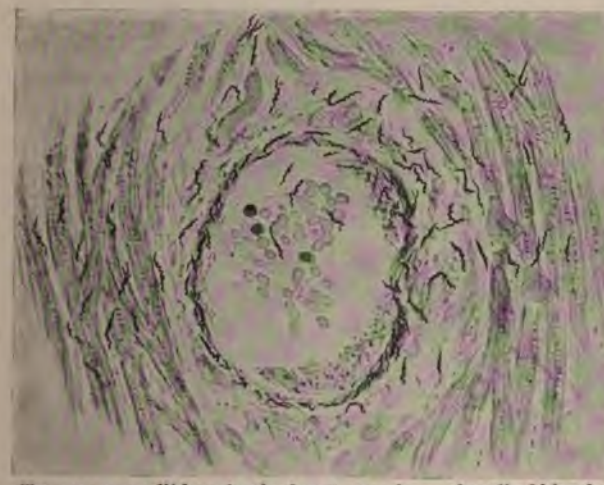


PLATE IV.—Treponema pallidum in the heart muscles and wall of blood vessel of man.

is found only in small numbers. In fetal prenatal syphilis the organism is present in large numbers in the liver, spleen, kidneys and other viscera of the fetus (Fig. 42 and Plate IV), as well as in the decidua and placental villi. The parasite can be successfully inoculated into certain of the lower animals.

Animal Inoculation.—In experimental inoculation when the organism of syphilis is injected into anthropoid apes, after an incubation period of from fifteen to fifty days (the average being thirty days), the primary lesions appear, and after from nineteen to sixty days (the average being about thirty days) the secondary symptoms occur. The organism is also infective for the lower monkeys as well as such animals as dogs, sheep, guinea-pigs and rabbits, but in these the infection results in a localized disturbance that bears no clinical resemblance to the syphilis of man.

Culture.—Under anaërobic conditions Noguchi has succeeded in obtaining pure cultures of *Treponema pallidum* that were pathogenic for susceptible animals. His cultural method is as follows: The medium employed consists of equal parts of nutrient agar, rendered slightly alkaline, and ascitic hydrocele fluid. The medium is kept fluid at 45° C., and a bit of aseptic fresh normal tissue, either from the testis or kidney, is placed at the bottom of the tube. The medium is covered with a column of sterile vaselin or paraffin oil about 3 cm. in height. The tube is incubated for forty-eight hours at 37° C., after which, if it is found to be free from contamination, the material to be studied is carefully deposited, with the aid of a pipet, in the substance of the tissue, care being observed not to introduce air during the manipulation. The tubes are then incubated at 37° C., and are examined at intervals. The culture usually manifests itself after the first or second week as a diffuse cloud.

As the first growth is generally impure because of the presence of contaminating organisms in the material used for inoculation, subsequent reinoculation into fresh medium is necessary in order to isolate the organism. Once the artificial growth has been started successfully, it may be maintained in bouillon or ascitic fluid to which a piece of sterile tissue has been added.

Differential Characteristics.—*Treponema pallidum* can be differentiated from *S. refringens*, with which it is commonly associated, by the following features: *T. pallidum* is not so easily stained, its spirals are preformed; numerous and equidistant from one another; there is no undulating membrane; the organism is extremely slender, and the terminal prolongation of the periplast forms a fine flagellum at one or at both ends.

Life History.—Reproduction takes place chiefly by direct longitudinal division, although it is possible that, in some instances trans-

verse division also occurs. The longitudinal division consists in a splitting of the flagellum; followed by division of the body, but it is probable that this is initiated by a primary segmentation of the chromatic substance of the parasite.

Male and female gametes and asexual reproduction by conjugation, encystment, and spore formation have been observed by some. It is also believed that spores are produced which, when carried by the blood, may develop into treponemas in parts distant from the site of the original or primary lesion. These views have not been satisfactorily demonstrated and are not generally accepted.

Mechanism of Infection.—The transmission of the parasite usually takes place by contact, especially during sexual intercourse. The infective stage of the parasite corresponds to the form generally found in the primary lesion. Direct infection may occur, although rarely, through abrasion of the skin or by means of a wound infected during a surgical operation. Transmission through the agency of insects—flies, mosquitoes, etc.—is uncommon. The organism is easily transmitted to the fetus by the mother, through the placenta.

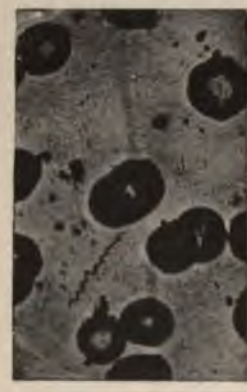


FIG. 43.—Treponema pertenue Castellani. (*After Castellani and Chalmers.*)

Pathogenesis.—*Treponema pallidum* is the cause of syphilis in man.

Treponema pertenue (Castellani, 1905).—*T. pertenue* is an organism so closely resembling *T. pallidum* as to be indistinguishable from it. It is variable in size, being from a few to 18 or 20μ in length. It is very slender and provided with numerous preformed spirals. Like *T. pallidum*, both ends are usually tapering, although forms having blunt or loop-like ends may occasionally be seen; there is no undulating membrane (Fig. 43).

Habitat.—The organism is found in the lesion of frambesia or "yaws," and also in the blood of persons affected with this disease.

Animal Inoculation.—Although yaws is a disease peculiar to man, it has been transmitted experimentally to the higher monkeys. Inoculation is usually made with the scrapings from the lesion. Symptoms develop after an incubation period of about one month. Castellani has succeeded in transmitting the disease to monkeys by inoculating them with blood obtained by splenic puncture. In these cases the incubation period lasted thirty-six days. According to the same author, only the primary lesion is produced in macaques, whereas in orang-outangs both the primary and the secondary lesions may be seen.

mmunity.—Monkeys immunized against yaws are not immune to ilis, and vice versa. Similarly, a man suffering from yaws may ire syphilis. The two microörganisms and the respective diseases ced by them, although closely allied, are entirely distinct. In an attack of yaws usually confers immunity against a second k, but this is not the case with syphilis. Man is, however, to be immune to reinfection with syphilis so long as he is syphili- but if, after successful treatment, he is freed from the disease and Wassermann reaction is negative, he becomes again susceptible infection with syphilis.



FIG. 44.—Frambesia (*Yaws*); second stage, general eruption.

Cultures.—The organism has been grown in artificial cultures by Noguchi, the same technic being employed as for the cultivation of *T. pallidum* (page 103).

Differential Characteristics.—*T. pertenue* so closely resembles *T. pallidum* that differentiation is dependent more upon a consideration of the foregoing facts than upon slight and inconstant morphologic variations.

Life History.—The life history of *T. pertenue* is the same as that of *T. pallidum*. Reproduction takes place by direct longitudinal division. Some observers have reported the finding of sexual forms, and

their conjugation has been described, but satisfactory confirmation is not at hand.

Mechanism of Infection.—The infective stage of the organism corresponds to the form usually found in the lesions of yaws. The disease is believed to be transmitted chiefly by contact, but insects, more especially flies, are regarded by some authorities as common carriers of the infection.

Pathogenesis.—*Treponema pertenue* is the cause of yaws, or frambesia, in man—a disease that is closely allied to syphilis (Fig. 44).

DIFFERENTIAL DIAGNOSIS BETWEEN SYPHILIS AND YAWS

Syphilis	Yaws
1. Primary lesion usually genital.	1. Primary lesion usually extragenital.
2. Eruption generally unaccompanied by pruritus.	2. Eruption generally accompaneid by pruritus.
3. Syphilis has a world-wide distribution.	3. Yaws is restricted to certain tropical countries.
4. An attack of syphilis does not confer immunity.	4. An attack of yaws usually confers immunity.
5. A syphilitic patient may contract yaws.	5. Patients suffering with yaws may contract syphilis.
6. Potassium iodid and salvarsan exert a less marked specific action.	6. Potassium iodid has a more specific action and with the use of salvarsan the disease disappears in two or three days.

The Wassermann test is a valuable aid in diagnosis.

II. FAMILY TRYPANOSOMIDÆ (Gruby, 1842)

History.—Morphology and Structure.—Habitat.—Animal Inoculation.—Immunity.—Agglutination.—Artificial Cultures.—Life History.—Mechanism of Transmission.—Pathogenesis.

The *Trypanosomidæ* are characterized by having a fusiform or elongated body, two nuclei (trophonucleus and kinetonucleus), a well-developed flagellum, and a distinct undulating membrane.

History.—The first trypanosome described was discovered by Valentin in the blood of a trout, *Salmo fario*, in 1841. Gruby, in 1842, was the first to employ the name *Trypanosoma*. He discovered a trypanosome, *T. rotatorum* in the blood of the frog. The trypanosoma of the rat, *T. lewisi*, was discovered by Lewis in 1878. In 1880 Evans isolated *T. evansi*, the cause of "surra" in the blood of diseased horses, mules, camels, and cattle.

Colonel Sir David and Lady Bruce in 1895 discovered *T. brucei* in the blood of animals, horses, asses, goats, etc., suffering from "tsetse-fly disease," or "nagana" (meaning weakness), and they also showed that the disease was transmitted by the bite of the infected tsetse-

fly, *Glossina morsitans*. Rouget, in 1894, discovered *Trypanosoma equiperdum*, the cause of a disease called "dourine" or "maladie du coit" in horses in Europe, India, northern Africa, and North America. This disease was transmitted by contact during coitus. In 1901 Elmassian discovered *T. equinum*, which was shown to be the cause of "mal de Caderas" in horses and dogs in South America.

Forde and Dutton, in 1902, found that *T. gambiense* was the cause of "sleeping sickness" in man, although this parasite was seen and imperfectly described prior to this time by Nepveu. Chagas in Brazil, in 1909, discovered *T. cruzi* in the intestine of *Lamus* (*Conorhinus*) *megistus* and in the blood of a child suffering from irregular fever, progressive anemia, etc. This organism is said to be the cause of a number of chronic affections known as "trypanosomiasis Americana," or disease of Chagas. This peculiar affection is most common in childhood, but also occurs in adults. Chagas likewise demonstrated the transmission of the disease by a bug,*Conorhinus sanguisugus* and allied species. Finally, in 1910, Stephens and Fantham described *T. rhodesiense*, the specific cause of a disease allied to sleeping sickness that is common in the northeastern part of Rhodesia and to the south of Lake Nyassa in Africa. The affection is transmitted by the bite of an infected fly, *Glossina morsitans*.

Morphology and Structure.—These organisms, as found in the blood of vertebrates, are usually of spindle shape, differentiated into ectoplasm and endoplasm, and provided with an undulating membrane and a well-formed flagellum. In the endoplasm of the parasite, when properly stained, two distinct chromatic masses can be distinguished. The first of these is the *trophonucleus*, improperly called macronucleus, concerned with nutrition; in the interior of this nucleus an achromatic body, the centrosome, can be seen. The other chromatic mass is the *kinetonucleus*, also improperly called micronucleus, which is concerned with locomotion. This nucleus is much smaller than the first, and is situated near the non-flagellated end of the parasite. From the kineto-nucleus a faint, poorly stained achromatic strand—the *rhizoplast*—may be seen; this ends in a minute, chromatic body—the *blepharoplast*—from which the flagellum arises. The blepharoplast is very indistinct and hard to see, and is probably absent in some cases (Fig. 36).

The flagellum is a chromatic structure that begins in the endoplasm. It has its origin in the blepharoplast, when this body is present, or, in case of its absence, in the kinetonucleus. In the latter case, however, it may be noticed that between the beginning of the flagellum and the kinetonucleus a very small intervening space is present, which is almost achromatic—the *rhizoplast*. The blepharoplast, though perhaps constantly present, is not always evident. The flagellum runs

outward from the endoplasm into the ectoplasm, then along the periplasm, which rises into a membrane—the undulating membrane—and finally projects as a free lash beyond the body of the parasite. The flagellum is therefore, composed of three parts—the *root*, in the endoplasm; the *undulating portion*, in the periplast, and the *free portion*. In some stages in the life cycle the flagellum may project directly from the ectoplasm through the periplast to the outside, and in such cases the ectoplasm enters only into the formation of a rudimentary undulating membrane (*Herpetomonas*), or this membrane may be entirely absent (*Crithidia*) (Fig. 64).

The undulating membrane is the layer of periplast raised by the periplastic portion of the flagellum. Not uncommonly it runs along a certain part of the free portion of the flagellum.

Habitat.—The trypanosomes are blood parasites, found abundantly among vertebrates in general. Some species have been described in fish, frogs, and reptiles and a few have been found in birds. Evolutional forms are commonly seen in blood-sucking insects—flies, fleas, mosquitos, ticks, bedbugs, etc., or in leeches, which, serve as intermediate hosts of the parasites.

Animal Inoculation.—The trypanosomes are easily transmitted into susceptible animals by inoculation of the parasitized blood. The material is obtained by collecting the infected blood in an isotonic citrate solution (2 to 4 per cent. in 0.85 salt solution), or by defibrination, and the inoculation is made by the aid of a pipet or syringe. Infection is more certain to take place if the inoculation is made intraperitoneally and if the same species of animal is used for performing the experiment. Thus, *T. lewisi*, which is easily transmitted to white or gray rats, is not transmissible to rabbits or guinea-pigs.

Immunity.—The protozoan infections are differentiated from the bacterial infections, by the fact that the former do not, as a rule, confer immunity after one attack. One species of trypanosoma, however, proves an exception to this rule. If a rat is inoculated with *T. lewisi*, the infection lasts for from a few weeks to about three months, and when the parasite disappears from the blood of the animal, the rat becomes immune to a second infection. That the immunity is a specific one is proved by the fact that the same rat is susceptible to infection by *T. brucei*. This same rule also applies to pathogenic species infecting the higher vertebrates. If a horse, after recovering from an affection induced by *T. evansi* (the cause of surra), so that its blood is no longer infectious for mice, be inoculated with *T. brucei* (the cause of tsetse disease, or nagana), the disease occurs with the same severity that it does in the control animal. When recovery from nagana takes place the aninal can be infected with *T. equiperdum* (the cause of mal de caderas), and so on. This fact is of great interest since it

serves as a point of differentiation between certain species that are almost identical morphologically.

Agglutination.—After infection, the serum of a rat immunized against *T. lewisi* will agglutinate the parasite. This agglutination is specific—that is, only *T. lewisi* is agglutinated.

Artificial Cultures.—McNeal and Novy were the first to succeed in the cultivation of trypanosomes *in vitro*. The culture-medium used by these investigators was blood agar, which is prepared by adding about one part of sterile defibrinated rabbit blood to about two parts of melted nutrient agar cooled to 45 to 50° C. The blood is mixed with the agar by rolling the tube between the fingers, and then is slanted and left in this position for about eight hours, or over night, so that hardening may take place. As a precautionary measure the tubes should be incubated at room temperature, but preferably at 37° C., for two or three days in order to obviate any bacterial contamination. A few drops of the parasitized blood are added to the water of condensation, and if this is not sufficient, a small quantity of sterile salt solution may be placed in the tube with a sterile pipet. The inoculated tubes are sealed by plugging them with cotton imbedded in a mixture of equal parts of paraffin and vaselin freshly melted. The culture is incubated at 37° C., or is left at room temperature in the dark for several days.

Artificial cultures of certain trypanosomes of mammals, as, *e.g.*, *T. theileri*, can readily be made on liquid media—thus the parasitized blood may be added to bouillon in the proportion of about two parts of the infected blood to five parts of bouillon (Miyajima).

In artificial cultivation the trypanosomes undergo great modifications, among which are a change in the polarity of the parasite and other morphologic deviations. The micronucleus and blepharoplast apparently migrate to the opposite end, and in consequence the undulating membrane is shortened or absent and the organism assumes the *herpetomonas* or the *crithidia* type respectively. Finally the parasite may become very dysmorphic and appear as an elongated, globular or ameboid body that varies in size.

Life History.—The life history of the *Trypanosomidæ* is not yet definitely known, and it is only in recent years that the evolution of some species that are parasitic to mammals has been studied. It has been shown that in the blood of vertebrates reproduction takes place by binary or multiple fission.

Study has revealed the fact that after a peritoneal or subcutaneous injection of parasitized blood into susceptible animals the trypanosome undergoes transformation at the point of inoculation and assumes the *crithidia* and *herpetomonas* forms preparatory to its entrance into the circulation. It is believed that such metamorphosis repre-

sents the evolutional or multiplication forms of the parasite. The same phenomenon occurs in the body of an intermediate host, such as an insect or a leech (natural medium), or upon artificial cultivation (blood agar). When, however, such evolutional forms are inoculated into the circulation of a susceptible host, the trypanosome type is

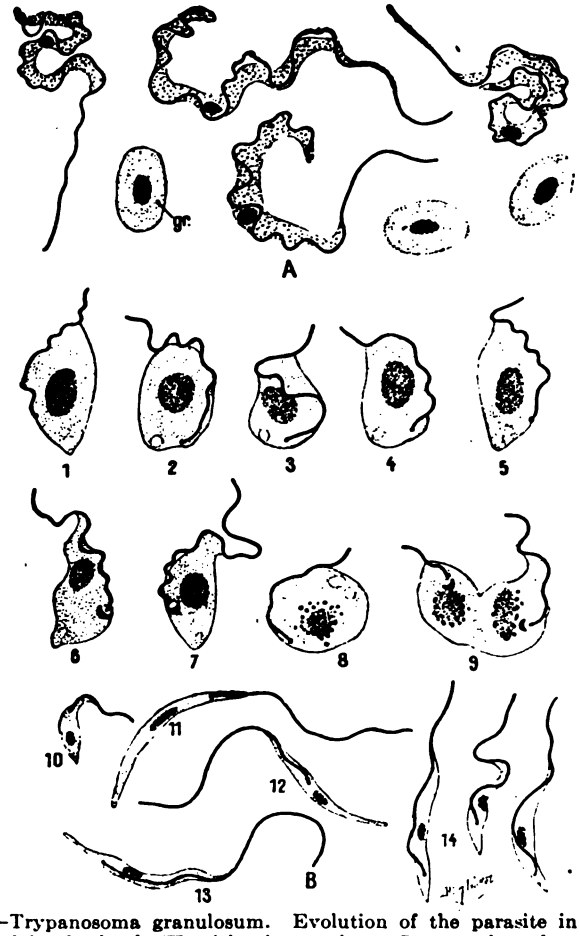


FIG. 45.—Trypanosoma granulosum. Evolution of the parasite in the body of the eel *A* and in the leech (Hemiclepsis marginata *B.gr.* nucleated erythrocyte; 1, 2, 3, 4 and 5, evolutional forms 3 hours after ingestion; 6 and 7, 5 hours after; 8 and 9, 7 hours after; 10, 11, 12 and 13, forms seen in the intestine; 14, metacyclic forms seen in the proboscis. (*After Brumpt.*)

again reverted to. Whether these evolutional forms represent phases of a sexual cycle or are merely examples of asexual multiplication has not as yet been determined, but it seems that such evolution in an intermediate host is essential, in most cases, for the transmission of the parasite to the vertebrate host, as is illustrated by the life cycle of some of the well-known species, such as follows:

Trypanosoma granulosum.—This trypanosome, discovered by Sabrazès and Muratet, is a parasite of the eel. According to Brumpt, its life cycle is as follows: The intermediate host is a leech, *Hemiclepsis marginata*, found in the neighborhood of Paris. The female adult lays from 50 to 80 eggs, and when hatched the young leeches attach themselves to the ventral surface of the mother. The leech procures nourishment for herself and her progeny by sucking the blood of an eel. If the fish is infected with trypanosomes, the parasites, on reaching the stomach of the young leeches, rapidly undergo transformation into *crithidia* and then into *herpetomonas*. After several days they reach the intestine, and finally, on the fourth day, small parasitic forms, *Trypanosoma metacyclique* (Brumpt), are found in the sheath

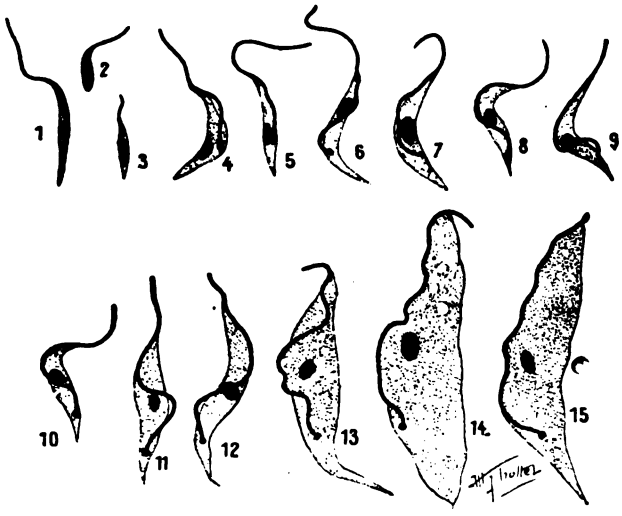


FIG. 46.—Trypanosoma inopinatum. Evolution of the parasite in the body of the leech Helobdello algera (1, 2, 3, 4, and 5) and in the frog (6 to 15) showing the great polymorphism of the flagellate. (*After Brumpt.*)

of the sucker. In this form the parasite is transmitted to another eel by the bite of the leech, and is found in the blood of the eel four or five days afterward. It is of interest to note that before entering the circulation these metacyclic forms of trypanosomes undergo multiplication at the point of inoculation. A similar metacyclic evolution has been demonstrated by Rhodain in the case of *T. brucei* (Fig. 45).

Trypanosoma inopinatum.—This trypanosome is a parasite of the frog, and is also transmitted by a leech, *Helobdella algira*. The evolution is similar to that of *T. granulosum*, except that the process takes place in the stomach (Fig. 46). In this variety, however, a transmission from the adult leech to the larva also takes place (Brumpt).

Among the parasitic trypanosomes of mammals a similar meta-

morphosis occurs, either by *direct fixation* when the evolution takes place either in the saliva of the proboscis, as in *T. cazalboui*, or by *indirect fixation* when the evolution takes place in the intestine, from which they pass to the salivary gland in the *metacyclic* form, as is the case with *T. gambiense, T. brucei*, etc.

Trypanosoma lewisi.—This organism is a parasite of the rat, and is transmitted by the flea (*Ceratophyllus fasciatus*). On being ingested with the blood by the flea when biting an infected rat, the trypanosomes undergo multiplication and evolution into *crithidia, herpetomonas*, and *metacyclic* forms in the posterior part of the intestine of the flea. These metacyclic or infective forms in turn pass forward into the mid gut and are regurgitated into the probosis. The flea, therefore, acts as an intermediate host. Infection takes place by the bite of the flea, but the parasite is not found in the salivary gland of this insect. Also by the rat swallowing the excrement from the infected flea.

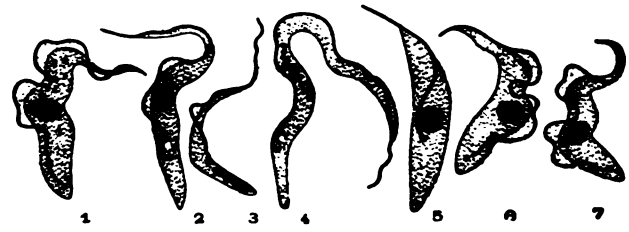


FIG. 47.—Trypanosoma Gambiensis. Evolution of the parasite in the body of Glossina palpalis. 1. common form as seen in the peripheral blood of man; 2, form seen in the middle intestine of the fly (33 days after); 3. rare crittridial forms as seen in the posterior portion of the intestine (46 days after); 4, slender forms seen in the anterior portion of the intestine (30 days after); 5, form seen in the posterior intestine (44 days); 6, metacyclic form seen in the salivary gland (34 days); 7, id (46 days) enlarged about 1500. (*After Bruce, Hamerton, Bateman and Muckis in Brumpt.*)

Trypanosoma cazalboui.—This organism, occurs as a parasite of the goat in French Guiana, and is transmitted by *Stomoxys bouffardi.* When ingested, the parasite undergoes evolution, but only in the salivary secretion in the proboscis of the insect, those that pass to the stomach being destroyed. This form of primitive evolution in the proboscis is called *evolution by direct fixation* (Rouband). The trypanosomes become transformed into *crithidia*, undergo multiplication, and after from six to ten days reach the infective stage. The parasite is now called the *salivary trypanosoma of Roubaud*, which corresponds to *T. metacyclic* of Brumpt previously described.

Trypanosoma gambiense, T. rhodesiense, T. cruzi, T. brucei, etc.—These trypanosomes, when ingested with the blood by an intermediate host, undergo the same cyclic evolution into *crithidia* and *herpetomonas*, that has just been described. This evolution takes place primarily in the digestive tract, and then as metacyclic forms, the organisms reach the proboscis through the salivary gland (Fig. 47).

Mechanism of Transmission.—Infection of trypanosomes may take place directly through an abrasion of the skin, a wound, or possibly by way of the digestive tract; or it may occur indirectly through the bite of an intermediate host, such as a blood-sucking insect, a leech, etc. In the latter case the parasite undergoes a cyclic evolution and multiplication either in the proboscis of the insect (*direct fixation*) or in the intestinal tract (*indirect fixation*). The metacyclic form represents the infective stage of the parasite, which is transmitted either by the bite of the infected insect (*T. gambiense*, etc.) or by the host swallowing the excrement of the insect which contains the metacyclic forms (*T. lewisi*) as already stated.

Pathogenesis.—The trypanosomes of mammals can be divided into two groups: (1) The non-pathogenic and (2) the pathogenic.

Non-pathogenic Trypanosomes.—These trypanosomes are represented by *T. lewisi*, and are characterized morphologically by the fact that the undulating membrane is less waved, and biologically they are distinguished by the fact that they are, as a rule, inoculable only into the same species; often the inoculation proves negative, but when positive, one infection usually confers immunity.

Pathogenic Trypanosomes.—The undulating membrane of the pathogenic trypanosomes is more waved than in the non-pathogenic variety, and the flagellum possesses characteristics that are sufficiently marked to make a differentiation into three groups possible; thus—(1) Those in which the flagellum is always complete, that is, composed of a root and an undulating and a free portion, as in *T. brucei*, *T. cruzi*, *T. equinum*, *T. evansi*, etc. (2) Those in which the free portion of the flagellum is absent, as in *T. congolense*, *T. dimorpha*, parasites of horses, cattle, etc. (3) Those in which the free portion of the flagellum may be present or absent, as in *T. gambiense*, *T. rhodesiense*, etc. Biologically, the pathogenic trypanosomes are characterized by the fact that they are inoculable into most laboratory animals, *T. theileri* and *T. cazalboui* being the exceptions. Man is usually resistant to all the trypanosomes except to *T. gambiense*, *T. rhodesiense*, and *T. cruzi*, which are known to be the causes of the sleeping sickness of Africa and of trypanosomiasis Americana respectively.

GENUS TRYPANOSOMA (Castellanella)

1. **Trypanosoma gambiense** (Dutton, 1902).—This parasite possesses the common characteristics of a pathogenic trypanosome. In size it is about 18 to 30 μ by 1.5 to 2.5 μ; in the young forms the micronucleus is sometimes close to the beginning of the flagellum, which not uncommonly may be incomplete.

History.—According to some authors, the credit for first having demonstrated the presence of trypanosomes in the blood of man in

Algeria is due to Nepveu, a finding that has not been confirmed. Forde and Dutton, in 1902, observed a flagellate in the blood of a patient suffering from irregular fever. This parasite was described by Dutton under the name of *T. gambiense*. Later Manson, and in 1903 Brumpt, corroborated Dutton's observations. In the same year Castellani discovered a trypanosome in the blood and spinal fluid of persons suffering from sleeping sickness in Uganda, and to this he gave the name of *T. ugandense*. These observations were confirmed by Bruce and Nabarro, Bettencourt, Todd, and others. Subsequent researches by Nabarro proved conclusively that the *T. gambiense* of Dutton was identical with the *T. ugandense* of Castellani, and that the sleeping sickness of man was the terminal stage of the irregular fever described by Forde and Dutton or the febrile trypanosomiasis of Brumpt.

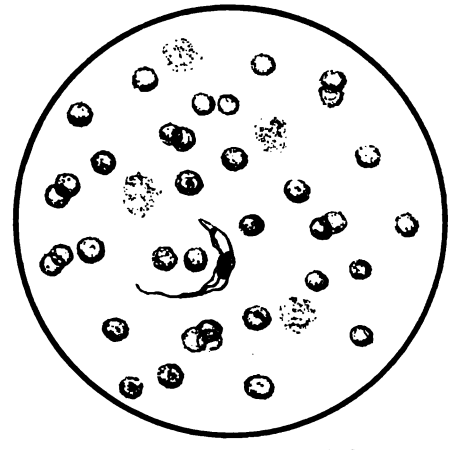


FIG. 48.—Trypanosoma gambiensis in human blood.

Habitat.—T. gambiense is found in the blood, cerebrospinal fluid and lymphatic glands of persons suffering from sleeping sickness. It may also be found in the intestinal tract, proboscis, and salivary glands of infected "tsetse flies," and also in the blood and spinal fluid of the laboratory animals inoculated with parasitized blood. Although man is probably the principal host for the reception of the virus, Bruce and others have shown that the parasite can be transmitted by the bite of an infected fly to antelopes and cattle; and since monkeys are also susceptible to the infection, it is probable that these and other vertebrates may serve as hosts for the reception of the virus.

Animal Inoculation.—With few exceptions most animals are susceptible to inoculation with *T. gambiense*. The disease is acute, of short duration, and usually terminates in death. The symptoms are the same as those produced by other pathogenic trypanosomes. In

some cases inoculation gives rise to a mild infection, but there is no relation between the virulence of the parasite in man and that in the lower animals.

Immunity.—Infection by *T. gambiense* in man and in the lower animals is usually fatal, although a few cases may recover spontaneously. A previous attack does not, however, confer immunity against a second infection.

Agglutination.—The serum of animals infected with *T. gambiense* is capable of agglutinating the parasite. This agglutination is specific for the parasite, and in the case of trypanosomiasis in the lower animals this reaction serves as a means of differential diagnosis from other pathogenic trypanosomes.

Cultures.—*Trypanosoma gambiense* is apparently strictly parasitic, and up to the present time artificial cultivation of the parasite has not been successful.

Life History.—*Trypanosoma gambiense* multiplies asexually by simple division. A sexual reproduction has been shown to take place in the intestinal tract of the intermediate host, the tsetse fly, but this has not been successfully demonstrated in the blood of man, where the parasite is usually rare. In man multiplication forms are rarely seen, except in the spinal fluid, but in the blood of rats, where the parasite occurs in great numbers, these forms are found without difficulty. They are seen to be undergoing longitudinal division, and not uncommonly forms with three, four, or even five flagella, corresponding to as many organisms, may be observed undergoing the process of division.

In the intestinal tract of the tsetse fly, *Glossina palpalis*, which acts as an intermediate host of the parasite, multiplication, with evolution into *crithidia*, *herpetomonas*, and *metacyclic* forms, takes place. In this evolutional stage they reach the salivary gland and proboscis, and when introduced into a susceptible host by the bite of the fly, the cycle is repeated. In the intermediate host, therefore, the cycle is by indirect fixation; that is, evolution takes place in the intestinal tract, from which the virus pass to the proboscis of the fly.

Mechanism of Infection.—Infection with *T. gambiense* by direct contact through an abrasion of the skin, wounds, etc., is rare. Artificially, the parasite may be transmitted to the lower animals by injection of parasitized blood subcutaneously, intraperitoneally, or intravenously. The parasite is transmitted to man by the tsetse fly, and the transmission is not purely mechanical, but evolutional (Klein). The infective stage is represented by the metacyclic form, as found in the salivary gland or proboscis of the fly. According to Klein, Bruce, Hamerton, Bateman, and Mackie, only a small number of flies become infected—one in 60 (or five in 100, Brumpt). That the transmission

is not purely mechanical is proved by the fact that the fly becomes infective only eighteen days after feeding on parasitized blood and is capable of remaining infective for ninety-six days thereafter.

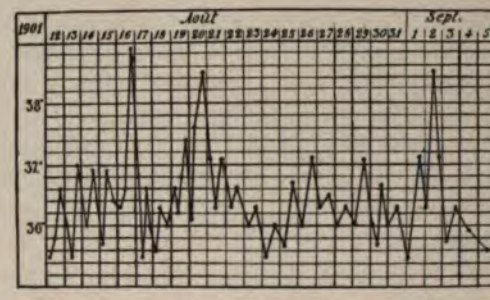


FIG. 49.—Temperature chart of sleeping sickness. (*Laveran and Mesnil.*)

Pathogenesis.—Trypanosoma gambiense is the cause of sleeping sickness in man—a disease that is common only in certain tropical regions of Africa. It is chronic in nature, and characterized at the outset by irregular fever; emaciation and physical and mental lethargy occur as the disease progresses. The prognosis is grave, for the dis-



FIG. 50.—Cerebral arteriole from case of sleeping sickness. Showing rich perivascular round cell infiltration.

ease is almost always fatal, although spontaneous recovery has been known to take place in some instances. A perivascular round-cell infiltration in the blood-vessels of the brain is a common lesion in this disease (Figs. 50 and 51).

2. **Trypanosoma rhodesiense** (Stephens and Fantham, 1910).—This trypanosome is probably identical with *T. gambiense*, which it

strongly resembles. *T. rhodesiense* is said to be differentiated from *T. gambiense* by the fact that the former is more polymorphic; by the appearance of small forms in which the undulating membrane is

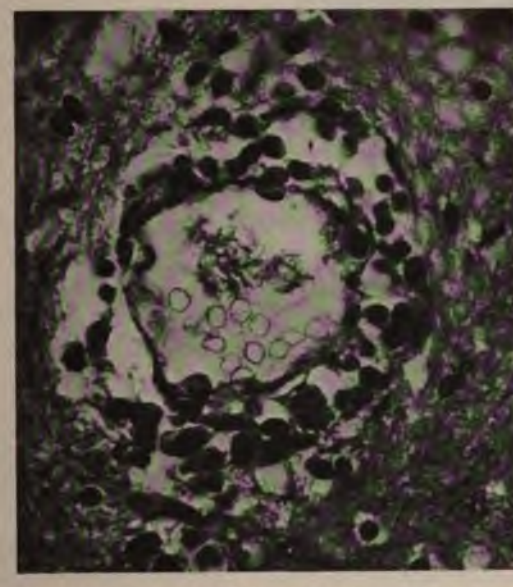


FIG. 51.—Cerebral arteriole from case of sleeping sickness, showing swelling of endothelium and perivascular lymphocytic infiltrate.

poorly waved and the micronucleus is in close proximity to the macronucleus. In some cases the position of the two nuclei is reversed, that is, the micronucleus is situated near the flagellated end of the parasite.

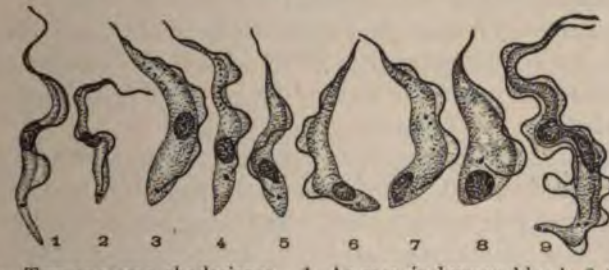


FIG. 52.—Trypanosoma rhodesiense. 1, As seen in human blood; 2 to 9, as seen in the blood of rat showing migration of the blepharoplast toward the flagellated or anterior part, in front of the trophonucleus (3 to 8) and division form (9) respectively. (*After Stephens and Fantham in Brumpt.*)

History.—In 1910 a trypanosome was found by Stephens and Fantham in cases of sleeping sickness in the northeastern part of Rhodesia and south of lake Nyanza. The fact that *Glossina palpalis* is not found in this region led Sanderson to advance the hypothesis

that this trypanosome differed from *T. gambiense*, and hence it was named *T. rhodesiense*. The researches of Yorke and the experiments of crossed immunization of Mesnil and Laveran have shown that this parasite has an individual entity.

Habitat.—This trypanosome is found in the blood of man in cases of sleeping sickness in Rhodesia. Kinghorn and Yorke have found the parasite in dogs and in antelopes in this part of Africa. The wild animals appear to be freely parasitized by this trypanosome, a fact that accounts for the difficulty in applying effective prophylactic measures.

Animal Inoculation.—Like *T. gambiense*, *T. rhodesiense* is inoculable in laboratory animals, the infection usually proving fatal.

Life History.—The multiplication of *T. rhodesiense*, like that of *T. gambiense*, takes place by longitudinal fission in the blood of the vertebrate. The intermediate host is *Glossina morsitans*, in the stomach of which, under favorable temperature conditions (about 28° C.), the parasite undergoes multiplication and evolution into *crithidia* and *metacyclic* forms in about twelve to fourteen days after infection. In these forms it reaches the salivary glands and proboscis and is inoculated into man by the bite of the fly.

Mechanism of Infection.—*T. rhodesiense* is transmitted to man by the bite of *Glossina morsitans*. The infective stage is the metacyclic form as found in the proboscis of the parasitized fly. The infection, it seems, is not merely mechanical, but evolutionary, requiring from twelve to fourteen days after feeding on parasitized blood for the fly to become infective; once infected, it remains in this condition for a long time. Since *T. rhodesiense* is commonly present in wild animals, it is not unusual to find flies infested with this parasite.

Pathogenesis.—*Trypanosoma rhodesiense* is the cause of sleeping sickness in the northeastern part of Rhodesia. The disease produced by this parasite is similar to that produced by *T. gambiense*, and it is probable that the two diseases are identical.

3. **Trypanosoma (Schizotrypanum) cruzi** (Chagas, 1909).—This trypanosome, found in the blood of vertebrates, resembles other pathogenic trypanosomes. It is actively motile, and about 20μ in length. It is differentiated from other trypanosomes by the fact that division forms are not seen in the blood. It is also peculiar in that it is found in the organs of the host, as, for instance, in the muscles in the leishmania variety.

History.—In 1909 the parasite was discovered by Chagas in the Institute Oswaldo Cruz, Rio Janeiro. It was found in the intestine of a bug, *Lamus* (*Conorhinus*) *megistus*, and also in the blood of a monkey infected by the bite of this insect. This led Chagas to investigate the possibility of the parasite being transmissible also to man and in the course of his research he found this flagellate to be the

cause of a number of acute and chronic diseases now known collectively as *trypanosomiasis Americana*, or *Chagas' disease*. The affection is usually grave, and more common among children than among adults.

Habitat.—The parasite is found in the blood of human beings affected with Chagas' disease. Evolutionary forms may be found in

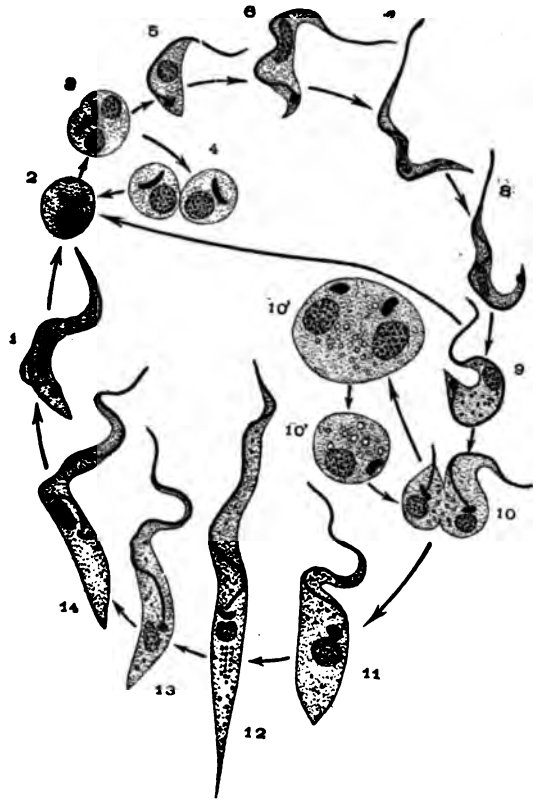


FIG. 53.—Evolution of Trypanosoma cruzi. 2 to 9, evolution in man and vertebrates; 9 to 14 and 1, evolution in conorhinus and cimex; 1, metacyclic or infective form for vertebrates; 2, 3 and 4, schizogonic forms in the organs; 5 to 9, evolution into adult trypanosoma; 9, 10, crithidial division forms found in the middle intestine; 10, leishmania forms often found in the stomach; 11 to 14, gradual transformation of crithidial (11) into metacyclic forms (1) in the posterior portion of the intestine. (*After Brumpt.*)

the intestinal tract of *Lamus* (*Conorhinus*) *megistus*. Since the parasite is inoculable experimentally in a large number of wild and domestic animals, it is probable that they act as carriers of the virus.

Animal Inoculations.—*T. cruzi* is inoculable in many domestic and wild animals, and also in those of the laboratory—dogs, cats, monkeys, guinea-pigs, mice, rats, rabbits, and chimpanzees.

Cultures.—*T. cruzi* has been cultivated artificially in blood a by Chagas, but Delana failed to obtain growth on retransplantati and according to Brumpt, the parasite cannot be cultivated artificia

Life History.—For the complete evolution of *T. cruzi* a vertebr and an invertebrate host are required. Reproduction takes pl chiefly asexually by fission, a peculiarity being that the parasite m tiplies in the internal organs or in the muscles and not in the blo



FIG. 54.—Trypanosoma (Schizotrypanum) cruzi. 4, leishmania forms in the cle of a rat infected experimentally; *M*, muscle fiber; *Ec*, endothelial cell lining a c lary. (× 1000 *after Brumpt.*)

with the result that, unlike other trypanosomes, division forms not found in the circulation. The sexual cycle of the parasite not been demonstrated.

The Cycle in the Vertebrate Host.—If blood parasitized with *cruzi* be injected into a susceptible animal, some of the paras become lodged in the muscles or internal organs; here they take leishmania form, undergo multiplication and cyclic evolution i

herpetomonas, finally assuming the trypanosome form and appearing as trypanosomes in the blood about five days after infection.

The Cycle in the Invertebrate Host.—The intermediate host of *T. cruzi* is an insect, *Lamus* (*Conorhinus*) *megistus*. In this insect the trypanosome undergoes multiplication and cyclic evolution in the stomach and intestine into *crithidia*, *herpetomonas*, and *metacyclic* forms respectively and reach the proboscis through the salivary gland.

Other species, such as *Conorhinus infestans*, *C. sordidus*, and *C. geniculatus;* the bedbugs, *Cimex lectularius*, *C. rotundatus*, and *C. baneti;* and the tick, *Ornithodoros*, may act as intermediate hosts for *T. cruzi*. Under favorable temperature conditions the insects become infective after from ten days to two weeks, and are capable of transmitting the parasite for from several months to over one year after infection has occurred. Under normal temperature conditions evolution does not take place during the months of December to February in the temperate region, which may perhaps explain why the disease is not propagated beyond the tropical regions.



FIG. 55.—American trypanosomiasis or Chagas' disease, acute form. The peripheral blood contained the parasite in great numbers. (*After Chagas in Brumpt.*)

Mechanism of Infection.—Men and animals are infected with *T. cruzi* through the bite of *Lamus megistus*, infected with the parasite. The parasite is infective in the metacyclic stage in the evolution of the trypanosome.

Pathogenesis.—The development of *T. cruzi* in man is the cause of trypanosomiasis Americana or Chagas' disease. The affection is common in the tropical regions of South America. Children are particularly susceptible to the disease, but adults are also affected. The prognosis is grave and the mortality high. It manifests itself either in acute or chronic form, and clinically it resembles thyroidism.

Pathogenic Trypanosomes of the Lower Animals.—T. evansi (Steel, 1885) is the cause of surra in horses in India. It is transmitted by the bite of flies (*Tabanides*) and probably also by fleas. The disease is characterized by fever, emaciation, edema of the limbs and ventral surfaces, lesions of the eye and eyelids, muscular weakness, paralysis, and death.

T. brucei (Plimmer and Bradford, 1889).—This trypanosome is the cause of "nagana," or tsetse-fly disease of horses and cattle in Africa. The virus is transmitted by several species of *Glossina*, especially *G. morsitans*. The disease is fatal to horses, asses, and dogs, but less



FIG. 56.—Trypanosoma evansi in rat blood.

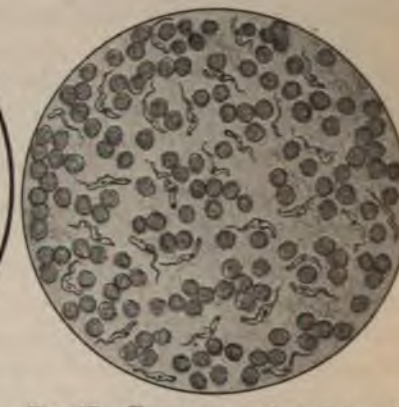


FIG. 57.—Trypanosoma brucei in rat blood.

virulent to cattle. It is characterized by fever, edema of the subcutaneous surface of the neck, abdomen, or extremities, hemolysis, and emaciation, and blindness is not uncommon. The parasite is always found in the blood.



FIG. 58.—Typanosoma equinum in rat blood.

T. equinum (Voges, 1901).—This parasite is the cause of "mal de caderas," a disease fatal to horses and dogs in South America. It is characterized by weakness, although the appetite remains unim-

paired, fever, staggering gait, paralysis of the hindquarters and dragging of the hind limbs, the hoofs scraping the ground. The horse staggers as it walks, the hindquarters swinging from side to side (hence the name, "mal de caderas," given to the disease). It terminates fatally about two months after the paralysis sets in. The parasite is found in the blood, and is inoculable into laboratory animals. It is differentiated from other trypanosomes by the extreme minuteness of the kinetonucleus. Transmission occurs probably through the medium of flies; dogs may, however, be infected by eating diseased animals.

T. equiperdum (Döflein, 1901).—This trypanosome is the cause of dourine, or "maladie du coit," a disease in horses of Europe, India, northern Africa, and North America. The incubation period is from

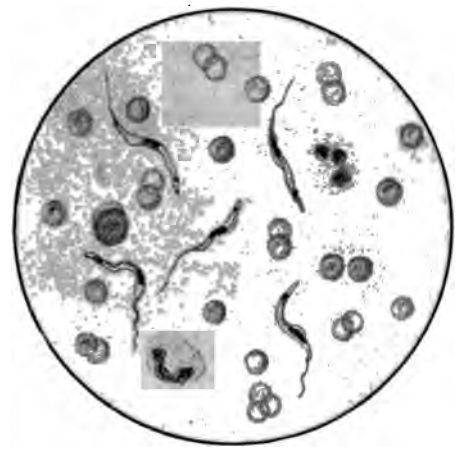


FIG. 59.—Trypanosoma equiperdum in rat blood.

eleven to twenty-one days. The disease is usually chronic in form, and is characterized by edema, without inflammation, of the genitalia, lasting about one month, and followed by emaciation and weakness. After about two months an eruption appears, as a rule, upon the sides and hindquarters; this is surrounded by edematous areas, and is accompanied by synovitis, enlargement of the lymph-glands, and mild fever. In the final stage the animal becomes markedly anemic and emaciated; there is difficult micturition, followed by softening of the spinal cord and paralysis. The infection is usually fatal, death taking place in about eighteen months after the onset. The disease may sometimes run an acute course, the animal dying within a month or two after infection has occurred.

The parasite is most readily obtained from the plaques accompanying the eruption. It is inoculable into laboratory animals. The

virus is usually transmitted by contact during coitus. In this respect the disease resembles syphilis.

T. dimorpha (Laveran and Mesnil, 1904).—This parasite is the cause of a disease attacking horses in Gambia and in other parts of Africa. It also affects cattle, dogs, sheep, and goats. The trypanosomes somewhat resemble a tadpole in shape. The organism has been cultivated artificially and is inoculable into laboratory animals. The disease manifests itself by weakness, fever, and edema of the abdomen and scrotum. Death occurs within about a year after infection. The virus is transmitted by different species of *Glossina*, especially by *Glossina palpalis*.

T. theileri (Bruce, 1902).—This trypanosome is the cause of "galziekte," or gall-sickness, in cattle in Africa and India. It has an incubation period of from three to five days. The disease may run an acute or a subacute course, and is characterized by fever, severe anemia, leukocytosis, and basophilia. It is often complicated by babesiasis or spirochetiasis. The trypanosome is of large size, from 60 to 70 by 4 to 5μ, but small forms may also be found (25 to 53 by 2 to 3μ). It is not inoculable into other animals. The virus is transmitted by *Hippobosca*, a pupiparous fly that feeds on horses and is sometimes called the winged tick fly of the horse.

T. cazalboui (Laveran, 1906).—This parasite is the cause of "souma" in goats and horses in West Africa. The virus is transmitted by different species of *Glossina*.

T. hippicum (Darling, 1910).—This organism is the cause of "murrain" in horses in Panama.

T. venezuelense.—This organism is the cause of "peste-boba" or "desrangardera" a disease of horses in Venezuela.

Other trypanosomes of less importance than those described are: **T. annamense,** found in horses in Annam and Tonkin; **T. soudanense,** the cause of "tahaga" in camels; **T. togolense,** a variety found in horses in Togoland; **T. congolense,** a species found in horses, cattle, and camels in the Congo; **T. pecaudi,** a species said to cause "baleri" in horses in the Soudan, etc.

The following is a short description of some of the most common non-pathogenic trypanosomes:

T. lewisi (Kent, 1880).—This trypanosome is found in the blood of the rat; it is cosmopolitan and widely distributed in nature. In some localities 50 per cent. of the rats may be found thus parasitized. It is more commonly found among young than among adult rats, since the older rats, having been previously infected become immune.

For general laboratory purposes, such as animal inoculation, studies in immunity and agglutination, artificial cultivation, etc., *Trypanosoma lewisi* offers excellent material for study. The parasite is usually

non-pathogenic, but in very young rats it may produce marked emaciation, retardation in growth, anemia, cachexia, and occasionally death (Rivas). The virus is transmitted by the flea. In the intestine of this insect the parasite undergoes development and cyclic evolution into *crithidia* and metacyclic forms, the latter, which represents the infective stage, reaches the proboscis by regurgitation and not through

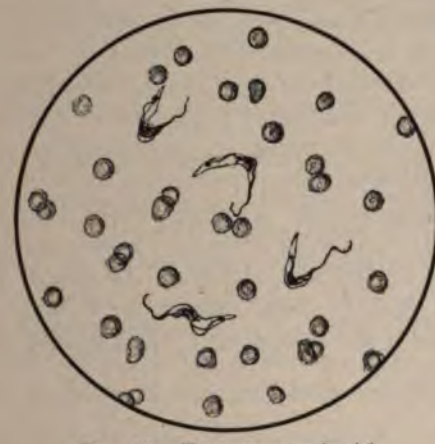


FIG. 60.—Trypanosoma lewisi.

the salivary gland. The parasite is transmitted to a new host through the bite of the flea.

T. rotatorium (Mayer, 1843).—A parasite occurring in several species of frogs. This trypanosome is characterized by its dysmorphism. Two main types, the flattened and the pectinated form are recognized, but many variations occur. The parasite may appear as



FIG. 61.—Diagram of trypanosoma rotatorium.

an ameboid, globular, oval or elongated organism. It is very actively motile, but is slow in progress. The undulating membrane is very prominent. This parasite is found in the blood of the frog, and offers excellent material for the study of the undulating membrane. The flagellum is sometimes rudimentary or absent.

T. duttoni (Thiroux, 1905).—This parasite is found in the mice of Senegal but is not inoculable into rats; it is said that it may pass the

placenta and multiply in the fetus. It is probably transmitted by fleas.

T. blanchardt (Brumpt, 1905).—A parasite found in the common dormouse. It is not inoculable into rats.

T. criceti (Luhe, 1906).—An organism found by Koch in 1881 in the hamster. It resembles *T. lewisi* but is not inoculable into rats. It is probably transmitted by the flea.

T. elephanti (Bruce, Hamerton, and Mackie, 1909).—A trypanosome found in the elephant. It resembles *T. brucei*.

A few trypanosomes have been found in birds; thus **T. avium** has been found in the wood owl; **T. paddæ**, in the Java sparrow, etc. Among the reptiles, **T. damoniæ** is found in an Asiatic tortoise (*Damonia revesi*); **T. pithonis** is found in the boa, etc. Among the fish, the first known trypanosome was found by Valentin in 1841 in the brown trout (*Salmo fario*). **T. rajæ** is found in *Raja punctata*, and several other species have been found in the eel (Brumpt), etc. Among the invertebrates, **T. gravi** and **T. tullochi** have been seen in *Glossina palpalis;* **T. culicis** in the mosquito, **T. christophersi** in the tick, etc.

GENUS TRYPANOPLASMA (Laveran and Mesnil, 1901)

Under the name trypanoplasma Laveran and Mesnil (emended 1904) described parasitic trypanosomes found in the blood and intestines of vertebrates. These were characterized by the presence of two flagella, one at each end, and having a kinetonucleus, the size of which is almost as large as the trophonucleus. These parasites offer good material for the study of the blepharoplasts, which are seen as two chromatin granules in front of the kinetonucleus. The one gives rise to the anterior and the other to the posterior flagellum, to which the undulating membrane is attached. These organisms possess additional interest since, as they are found in the alimentary canal and also in the blood (Leger and Keysselitz), they may possibly represent an intermediate stage of parasitic evolution among flagellates.

Reproduction occurs asexually by longitudinal fission, the division of the kinetonucleus preceding that of the flagellum. Sexual reproduction is believed to take place in an intermediate host, probably a leech, a fact that has never been demonstrated.

Trypanoplasma intestinalis (Leyer, 1905).—This flagellate is of interest since it was the first trypanosome-like organism to be found outside of the blood. It is a parasite of the alimentary tract of *Box boöps*, a salt-water fish. Globular forms have been described by Leyer. Forms having three flagella, and resembling *Trichomonas*, and others with a rudimentary undulating membrane may also be seen. Other trypanoplasms have been described in fish and leeches, as, *e.g.*, **T. ventriculi**, in *Cyclopterus lumpus;* **T. truttæ** in the trout

(*Salmo fario*); **T. abramidis** in the bream (*Abramis brama*) and the leech (Pisciola), etc.

GENUS TRYPANOPHIS (Keysselitz, 1904)

The trypanophis resembles the trypanoplasm in having two flagella, but is differentiated from the latter by the fact that the kinetonucleus is much smaller than the trophonucleus.

Trypanophis grobbeni (Poche, 1903).—This parasite is found in the gastric cavity of various *Siphonophora*.

Endotrypanum (Mesnil and Brimont, 1908).—This parasite is a type intermediate between *trypanosoma* and *hemogregarina*.

GENUS HERPETOMONAS (Kent, 1878)

Though not parasitic in man, the known species of *Herpetomonas* are of interest because of their resemblance to the evolutional forms of trypanosomes. They are differentiated from trypanosomes by the absence of the undulating membrane. As a rule they are elongate or spindle in shape and are provided with a single flagellum. Like other *Binucleata*, they contain a trophonucleus and a kinetonucleus, the



FIG. 62.—Herpetomonas ctenocephali of the dog flea. 1, 2, 3, 7 and 8, herpetromonas forms free or aglutinated; 4, 5 and 6, division forms. (× 1500 *after Brumpt.*)

latter being situated near the flagellated end of the body. The flagellum becomes free by projecting directly through the ectoplasm, and in consequence the undulating membrane is absent.

Habitat.—Numerous species of *Herpetomonas* have been described. The majority of these are found in the digestive tract of the invertebrates, particularly among insects. The parasite becomes encysted in the intestine of the insect, and in this stage is discharged with the feces. Infection is believed to take place directly from one host to another, as in the case of *Ameba* and *Coccidia*. The *Herpetomonas* found in the intestine should not be confounded with the evolutional forms of *Trypanosoma*. They are differentiated by the fact that the evolutional forms of trypanosomes do not undergo encystment; not uncommonly they are associated with the metacyclic forms of the parasite.

Among the best known species of *Herpetomonas* found in invertebrates may be mentioned: *H. muscæ domestica*, found in the intestine of the house-fly; *H.* (*Crithidia*) *minuta*, found in *Tabanus tergestinus;* *H. ctenocephali*, seen in the dog flea (*Ctenocephalus canis*). Other species have been found in the intestine of mosquitos, etc. Recently, Franchini claimed to have found *H. brasiliensis* in the blood of man.

Life History.—Prowazek describes asexual reproduction by longitudinal division in *H. muscæ domestica*. The division begins in the trophonucleus, and is followed by division of the kinetonucleus and finally of the flagellum. This same observer also describes sexual reproduction, but this was not found to occur by Patton. Both authors describe encysted forms or resting stages, and agree that infection takes place directly by the feces.



FIG. 63.—Herpetomonas brasiliensis. 1, 2, 3 and 4, common forms; 5, containing several blephoroplasts and bacteria; 6 and 8, formation of peripheral grains (pre-encystment stage); 7 to 13, several encysted forms. (*After Franchini in Brumpt.*)

Pathogenesis.—All the well-known herpetomonas lead a saprozoic life in the lumen or the intestine or in the Malpighian tubules of insects.

GENUS CRITHIDIA (Leger, 1902)

In 1902 Leger found these flagellates in the intestine of the mosquito, *Anopheles maculipennis*. Morphologically, the *Crithidia* resemble the *Trypanosoma*, but are differentiated from the latter by the undulating membrane, which in the *Crithidia* is only rudimentary. The flagellate also resembles a herpetomonas, but in this parasite the undulating membrane is entirely absent, and the kinetonucleus is situated some distance from the trophonucleus toward the flagellated end of the parasite, whereas in *Crithidia* it is very close to the trophonucleus, but never toward the non-flagellated end. This parasite should also be differentiated from *Crithidia* forms of *Trypanosoma* (Fig. 64).

Habitat.—The *Crithidia* inhabit the intestine of invertebrates, especially insects. Some of the best-known species are: *C. gerridis*, found in *Gerris passarum; C. melophagia*, occurring in *Melophagus ovinus; C. fasciculata*, seen in *Anopheles maculipennis; C. minuta*, found in *Tabanus tergestinus*, etc.

Life History.—The life history of *Crithidia gerridis* is described by Patton as follows: The parasite, as found in the crop of the insect

(*Gerris passarum*), appears as a round or oval body, provided with a rudimentary flagellum. The asexual reproduction is by fission, and takes place in the crop. It begins first by division of the kinetonucleus, followed by splitting of the flagellum, so that two kinetonuclei and two rudimentary flagella are formed. The trophonucleus now divides, and two daughter cells are formed, which in turn divide, forming rosets of several individuals. The rosets break up, and the parasites being set free, elongate and undergo rapid longitudinal division. The parasites now pass to the intestine, where they become shortened and take the shape of a round body provided with a long flagellum. The flagellum then becomes absorbed and eventually de-

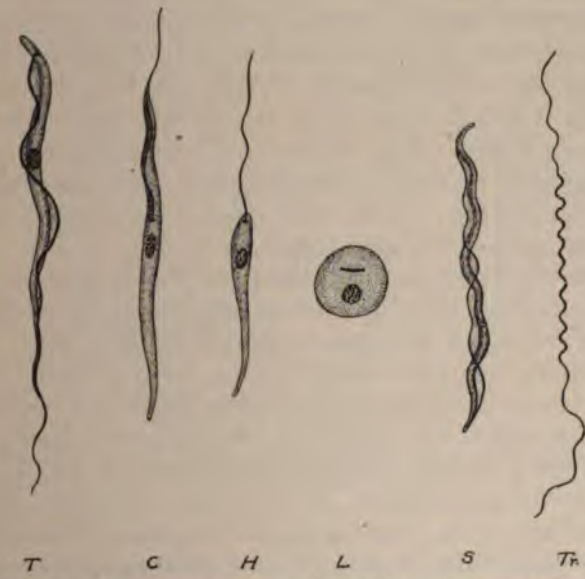


FIG. 64.—Diagram of *T.* trypanosoma; *B*, crithidia; *H*, herpetomona; *L*, Leishmania; *S*, spirochæta and *Tr.* treponema.

tached, and the organism takes the original form of a round body with a trophonucleus and a kinetonucleus and a rudimentary flagellum. In this stage the parasites are discharged with the feces in water, and the cycle is repeated when these bodies are taken up by a new host.

Mechanism of Infection.—Infection takes place by contamination of the water with the evolutional forms of the *Crithidia*, as found in the intestine, in the form of round bodies with a rudimentary flagellum. This stage, therefore, represents the infective stage of the parasite.

Pathogenesis.—Several species of *Crithidia* have been found in invertebrates, but none has been seen in man.

GENUS LEISHMANIA (Ross, 1903)

The parasites of this genus bear a strong resemblance to the trypanosomes, except that they have no undulating membrane at any stage of development. They live chiefly inside of endothelial cells, but may also be found in leukocytes or within the cells of the internal organs, such as the liver, spleen, etc.

In the intracellular stage the Leishmania appear as non-flagellated, small, oval, cytoplasmic bodies provided with a trophonucleus and a kinetonucleus. In the endocellular stage the parasite loses the flagellum, but in artificial culture it is seen to reappear.

Habitat.—The parasite has been found in man, horses, rabbits, and other mammals inside of the endothelial cells of the capillaries of the liver, spleen, bone-marrow, and lymphatic glands. It has also been observed in the mucosa of the intestine, in the leukocytes from the blood of the large veins (femoral, portal, and hepatic), and shortly before death it is found free in the peripheral blood. The parasites liberated from the cells may be taken up by the leukocytes and possibly by the erythrocytes. Experimentally the Leishmania may develop in the bedbug (*Cimex rotundatus*, Patton), and possibly in other insects, such as mosquitos, fleas, etc.

Cultures.—Some of the Leishmania, such as *L. donovani*, *L. brasiliensis*, *L. infantum*, have been artificially cultivated on blood-agar; under these conditions the parasite regains the flagellum.

Life History.—In man multiplication takes place intracellularly by simple binary fission and by multiple division into several individuals. In artificial culture the same division takes place and flagellated forms are produced. According to Patton, in insects, the same flagellated forms are produced as in artificial cultures. Flagellation may proceed at once and the parasite divide longitudinally, giving rise to two flagellated individuals; this same division may continue for a length of time; or instead of flagellation proceeding directly, the nuclei may multiply primarily without division of the cytoplasm, and give rise to a protoplasmic mass containing from eight to ten nuclei, which eventually breaks up into flagellated forms.

Mechanism of Infection.—The infection may take place by direct contact, as in Oriental sore (*L. furunculosa*), and possibly through an intermediate host, an insect, as in *Leishmania donovani*, *L. infantum*, etc.

Pathogenesis.—The *Leishmania* are the cause of certain important diseases in man, such as kala-azar (*L. donovani*); Oriental sore (*L. furunculosa*); infantile splenic leishmaniasis (*L. infantum*), etc. Five species of Leishmania known to be pathogenic to man have been described; *L. donovani*, *L. furunculosa*, *L. infantum*, *L. nilotica*, and *L. brasiliensis*.

1. **Leishmania donovani** (Laveran and Mesnil, 1903).—This parasite is usually found intracellularly in the endothelial cells as a round, oval, or pyriform body, measuring from 2 to 4μ by 1.5 to 2μ. Smaller forms may be found in cases of severe infection. The protoplasm is granular, and when properly stained by Romanowsky's method, is found to contain two nuclear structures—one large and round, the trophonucleus, usually situated toward the center, and the other small and bacillary in shape, the kinetonucleus, situated near the periphery of the cytoplasm. From the kinetonucleus a clear linear structure—the rhizoplast—at times runs toward the edge of the parasite, and a vacuole may also be seen (Figs. 64 and 65).

History.—Leishman, in 1900, found the organism at autopsy in a case of kala-azar in Calcutta, and Donovan found the same organism in 1903 in blood obtained by splenic puncture from patients suffering from the disease. In 1904, Rogers, by incubating the blood at 22° C.,



FIG. 65.—Leishmania donovani. Flagellated forms as seen in artificial cultures (*After Leishman in Brumpt.*)

observed the development *in vitro* of the parasite into flagellate forms. Christophers, in 1904, added considerably to the knowledge of this organism, and Patton, in 1905, showed that the parasite was found not only in the leukocytes, but also within the endothelial cells and in other cells of the internal organs. The last-named author also demonstrated the development of the parasite in the bedbug. Recently Row has been able to cultivate the parasite artificially in blood-agar.

Our present knowledge concerning this parasite shows that it is the cause of kala-azar, or tropical splenomegaly, and that the disease is probably transmitted by some insect.

Habitat.—Up to the present *L. donovani* has been found only in man. As a rule, the organism inhabits the endothelial cells, but it may also be found in the mononuclear leukocytes and occasionally in the polynuclear leukocytes. In preparations made from the spleen or liver (Fig. 66 and 67) the parasites may be found free in large numbers, but this is due probably to the breaking down of the cell during

manipulation. In severe infection almost every part of the body invaded, and during the febrile stage, and especially toward the e of the disease, the organisms are present in the leukocytes of the peri eral blood, and not uncommonly are free in the plasma. In expe

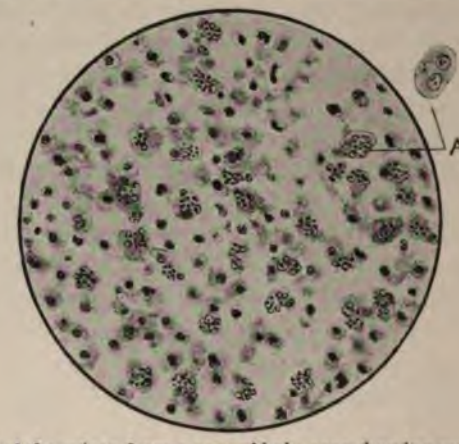


FIG. 66.—Section of the spleen from a case of kala-azar showing several parasites w the endothelial cells at *A*.

ments the parasite multiplies in the body of some insect, such as bedbug, mosquito, etc.

Animal Inoculation.—The virus is not inoculable in the lo animals.



FIG. 67.—Section of the liver from a case of kala-azar showing the parasites within t endothelial cells at *A* and in some of the liver cells at *B*.

Cultures.—Artificial cultures on blood-agar have recently be obtained by Row (Fig. 65).

Life History.—Multiplication inside of the body takes place b binary or multiple fission. In artificial cultures and in the body

such insects as the bedbug the parasite undergoes multiplication and evolution into elongated forms. The organism may give rise directly to a flagellate that subsequently divides longitudinally by binary fission, or this process may be preceded by a primary division of the nuclei without division of the cytoplasm, followed by the formation of large cytoplasmic masses containing several nuclei that eventually break up into separate flagellated forms (Fig 65).

Mechanism of Infection.—The mode of infection is not well understood, but it is possible that the virus may be transmitted by contact through abrasions or wounds of the skin. Since the disease is accompanied by ulceration of the mouth and of the mucosa of the intestine, this would also suggest the possibility of the virus being transmitted by contact, contaminated food or water, etc. There is some probability that the disease is transmitted by the bedbug, flea, mosquito, or other insects.

Pathogenesis.—The development of *Leishmania donovani* in man gives rise to a subacute or chronic specific febrile disease known as "kala-azar," "dumdum fever," or tropical febrile splenomegaly. It is accompanied at times by ulceration of the intestine and dysenteric symptoms, and is usually fatal.

Histoplasma capsulatum (Darling, 1906).—This organism was seen by Darling in Panama. It is oval or round in shape, from 1 to 4μ in diameter, and is usually inclosed in an achromatic capsule. It consists of a cytoplasm with achromatic spaces containing a single nucleus. This solitary nucleus serves as a point in the differentiation between this parasite and *L. donovani.*

Habitat.—The parasite is found in man in the endothelial cells of the capillaries and small blood-vessels of the liver, spleen, lungs, intestine, lymphatic glands, and leukocytes. Darling discovered flagellated forms in spreads made from the lungs and spleen.

Pathogenesis.—The parasite is said to be the cause of a form of splenomegaly that resembles kala-azar.

2. **Leishmania furunculosa** (von Firth, 1891) L. tropica (Wright, 1903).—Morphologically this parasite is identical with *L. donovani.* It is found within the endothelial cells and leukocytes as a round or oval body, and is provided with a trophonucleus and a kinetonucleus (Fig. 68 and Plate V).

Habitat.—In man the parasite inhabits by preference the endothelial cells or leukocytes. According to Manson and Gombault, it is also found in dogs. In laboratory experiments, multiplication and evolution of the parasite have been observed in the digestive tract of some insects, such as mosquitos, bedbugs, fleas, etc. (Wenyon).

Animal Inoculation.—The virus is inoculable from man to dogs and monkeys (Macacus sinicus), in which animals it produces ulceration of the skin which is of short duration (Nicolle).

Cultures.—According to Nicolle, the parasite can be cultivated artificially in glucose-blood-agar. In this medium the organism assumes the flagellated form.

Life History.—The evolution of *L. furunculosa* is similar to that of *L. donovani.* Multiplication takes place by simple binary or multiple fission inside of the cell. In artificial cultures the parasite becomes flagellated. Multiplication and evolution have been observed in several insects, as, for example, mosquitos, fleas, Pediculus vestimenti, etc.

Mechanism of Infection.—The virus may be transmitted by direct contact through an abrasion or wound in the skin. Transmission by insects may be possible, but has not been satisfactorily demonstrated.

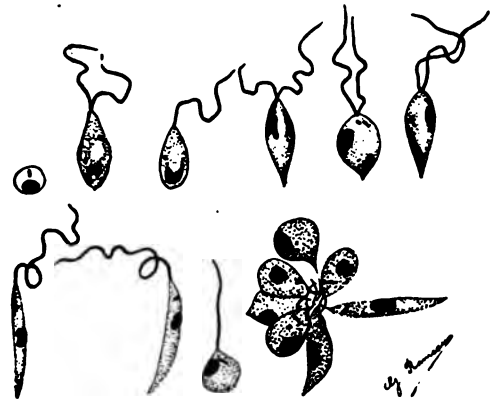


FIG. 68.—Leishmania furunculosa, forms seen in artificial cultures. (*After Ch. Nicolle in Brumpt.*)

Pathogenesis.—Leishmania furunculosa is the cause of Oriental sore, a specific, circumscribed, ulcerative affection of the skin. The disease is of short duration, lasting about one year, and one attack usually confers immunity. It occurs most commonly in the north of Africa and Egypt, Asia Minor, and Arabia, but has also been seen in Brazil, Panama and Mexico (Yucatan).

3. **Leishmania infantum** (Nicolle, 1908).—Morphologically *L. infantum* is identical with *L. donovani.*

Habitat.—This parasite was found by Pianese and Nicolle in children in Italy. Dogs and cats are most often affected and in certain places in Italy 80 per cent. of the dogs have been found thus parasitized, a fact that would tend to show that the dog is the natural repository for the parasite, its occurrence in children being probably merely accidental.

Animal Inoculation.—Dogs and monkeys are susceptible to the infection. Cats, guinea-pigs and mice, may be inoculated, but only

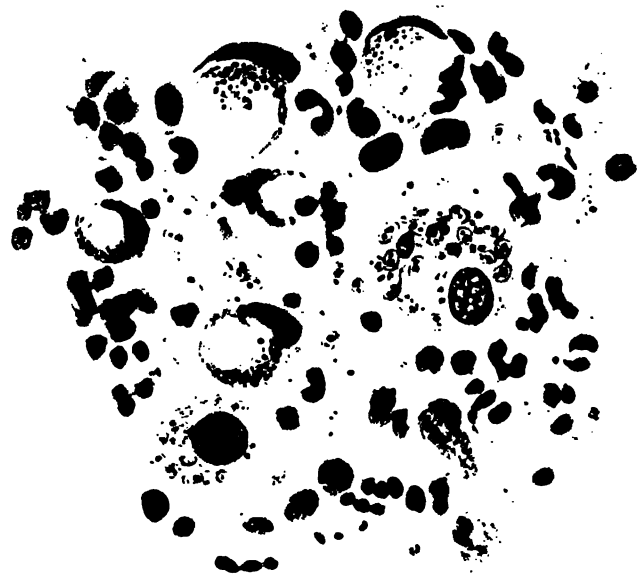


PLATE V.—Leishmania tropica.

with difficulty. In making the inoculation the infected material should preferably be taken either from animals or man, and not from artificial cultures.

Cultures.—Nicolle has succeeded in cultivating the parasite in blood-agar.

Life History.—The life history of *L. infantum* is somewhat obscure, but it is probable that, like *L. donovani* and *L. furunculosa*, division takes place by simple or multiple binary fission. Multiplication and cyclic evolution have been said by Basile, Sangiori, Alvarez, and Silva to take place in the flea (*Ctenocephalus canis*).

Mechanism of Infection.—Basile and Visentini have succeeded in transmitting the disease to young dogs through the bite of the flea, and it is probable that the virus is transmitted to children in the same way.

Pathogenesis.—*Leishmania infantum* is the cause of infantile kala-azar, a fatal disease of children. Clinically the affection can hardly be differentiated from kala-azar, except from the fact that it is more common in childhood, occurring between the ages of one and six years. The disease usually manifests itself by irregular fever, which does not subside under the administration of quinin, and is followed by marked anemia, enlargement of the spleen and liver, edema of the face and hands, subcutaneous hemorrhage, and general emaciation. Intestinal and cutaneous ulcerations, which are common in kala-azar, are absent in this disease. It runs a course of from a few months to several years, and usually terminates in death.

4. **Leishmania brasiliensis** (Vianna, 1911).—Morphologically this parasite is identical with *L. furunculosa*. It is the cause of leishmaniasis americana which probably is the same as Oriental sore.

Habitat.—The parasite is found in the lesion of the skin or mucous membrane, but in fewer numbers than in cases of Oriental sore. It is frequently found in the mononuclear leukocytes. Flagellated forms are occasionally seen.

Animal Inoculation.—The virus has been transmitted to dogs by direct inoculation of the cultures (Wenyon).

Cultures.—The parasite is easily cultivated on blood-agar (Pedroso, Silva, Wenyon, Lindenberg).

Life History.—The life cycle of *L. brasiliensis* is not clearly understood, but it is probably similar to the *Leishmaniæ* previously described. Multiplication and evolution are believed to take place in some insects as, *e.g.*, mosquitos, conorhinus, ticks, etc.

Mechanism of Infection.—While this is not understood, the virus is probably transmitted to man through the medium of an insect.

Pathogenesis.—*Leishmania brasiliensis* is the cause of *leishmaniasis americana*, also known as *forest yaws*, *bouba brasiliana*, etc. The

disease is common in Brazil, but has also been found in Panama, Yucatan, and elsewhere. It is an affection of the skin and mucous membrane of the nose and throat and is characterized by ulceration of the affected area.

5. **Leishmania nilotica** (Brumpt, 1913).—This parasite resembles *L. furunculosa*. It was found by Thomas and Balfour in Egypt, and is regarded as the cause of a nodular, non-ulcerative affection of the skin somewhat resembling keloid. These investigators have suggested the name "*Leishman's nodules*" for this disease.

III. FAMILY CERCOMONIDÆ (Kent)

Varieties.—(1) Cercomonas hominis; (2) C. longicauda; (3) Prowazekia asiatica; (4) Trichomonas vaginalis; (5) T. intestinalis; (6) T. pulmonalis; (7) Tetramitus mesnili.

Morphologically, the Cercomonidæ are round, oval, or pear-shaped protozoa provided with one or several flagella. With few exceptions they are binucleated. Some species are provided with a cytostoma, or gullet, located at the base of the flagellum, for the reception of food; others have a distinct undulating membrane. This family comprises four genera, namely, *Cercomonas*, *Prowazekia*, *Trichomonas*, and *Tetramitus*. Several species are parasitic to man, and most of them inhabit the intestine.

GENUS CERCOMONAS (Dujardin, 1841)

The cercomonades are small protozoa, round or oval in shape, from 8 to 10μ in length, and provided with a single flagellum. They possess neither undulating membrane, kinetonucleus, nor contractile vacuole. The cytoplasm contains only one nucleus, which is usually small and indistinct, and is situated eccentrically and near the flagellated end of the organism. These parasites are frequently confounded with *Trichomonas;* the fact, however, that the latter possess an undulating membrane and three or four flagella is an important point in the differentiation.

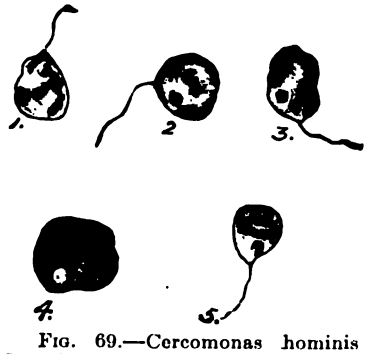


FIG. 69.—Cercomonas hominis Davaine. 1–3, and 5, flagellate forms; 4, encysted form. (*After Castellani and Chalmers.*)

1. **Cercomonas hominis** (Davaine, 1854).—This parasite was found by Davaine in the evacuations of cholera patients. Other observers have found it in the sputum in cases of pleural exudation and gangrene of the lung. It has also been seen in the lower animals, such as ducks and other fowl, etc. The common habitat of the parasite is the small intestine of man.

2. Cercomonas longicauda (Dujardin).—This parasite has been found in feces. It is distinguished by the presence of two flagella, one of which is very long and the other rudimentary. It undergoes encystment, and this probably represents the infective stage. The pathogenesis of the parasite has not been determined.

GENUS PROWAZEKIA (Hartman and Chagas, 1910)

The *Prowazekia* are oval or pyriform flagellates, characterized by the presence of two well-developed flagella and two nuclei—a trophonucleus and a kinetonucleus. Three species, *P. asiatica*, *P. cruzi*, and *P. weinbergi*, have been described. They are parasites inhabiting the intestine of man, but their pathogenesis is not well understood.

Prowazekia asiatica (Castellani and Chalmers, 1910).—This parasite was found in the feces of a case of ankylostomiasis. The organism has been cultivated artificially on agar. Multiplication takes place by binary fission, and encystment has been observed.

Prowazekia cruzi (Hartman and Chagas) and **P. weinbergi** (Mathis and Léger, 1910) are probably identical with *P. asiatica*.

GENUS TRICHOMONAS (Downs, 1837)

The trichomonades are round or pyriform in shape when at rest or when seen in stained preparations, but vary in shape, when active and in fresh preparations. They are differentiated from *Cercomonas* by the fact that they are provided with three or four flagella and a kinetonucleus, and by their larger size. The chief characteristic of *Trichomonas* is the presence of an undulating membrane. The species known to be parasitic in man are *T. vaginalis*, *T. intestinalis*, and *T. pulmonalis*.

1. Trichomonas vaginalis (Downs, 1837).—This parasite is fusiform or pyriform in shape, and from 15 to 25 by 7 to 12μ in size. It is provided with two nuclei, three flagella, all originating from the same point, and an undulating membrane. At times three instead of four flagella may be seen, the fourth flagellum taking the place of the undulating membrane, which is absent in these forms. Ordinarily the organism is found in the vagina, especially when the vaginal secretions are acid in reaction; it is not very common, however, since it is found in only about 10 per cent. of cases. It has also been found in the urethra and bladder of man, and in cases of gonorrheal vaginitis and other affections of the female genital organs, but no positive evidence has been adduced to prove that the parasite is the cause of the infection. The organism cannot be inoculated into the lower animals, nor has it been artificallly cultivated.

2. Trichomonas intestinalis (Leuckart, 1879).—*Trichomonas intestinalis*, also known as *T. hominis* or *Cercomonas hominis* (Davaine,

1854), is almost identical with *T. vaginalis*, from which it can be differentiated only by the fact that it has four instead of three flagella. The presence of an undulating membrane is characteristic of *T. vaginalis*, but as this membrane is usually absent when the organism is provided with four flagella, this accounts for the fact that the two parasites are often confused with each other.

The parasite measures 10 to 15 by 7 to 10μ and is found in the normal mouth and in the intestine of man in cases of diarrhea. It is not uncommonly associated with amebas. It is inoculable from man to monkeys and from monkeys to pigs.

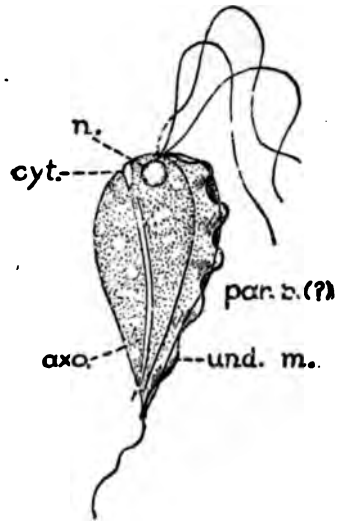


FIG. 70.—Trichomonas hominis (intestinalis); *n*, nucleus; *cyt*, cystostoma; *axo*, axostyle; *par. b*, para-basal body (?); *und. m*, undulating membrane. × 2400. (*After Wenyon in Chandler.*)

3. **Trichomonas Pulmonalis** (Schmidt, 1895).—This parasite has been found by several investigators in the sputum and lungs, in cases of phthisis, pulmonary gangrene, and putrid bronchitis.

GENUS TETRAMITUS (Perty, 1852)

The *Tetramiti* are flagellates characterized by the presence of a cytostoma. They have three flagella, all inserted near the same point and anteriorly, near the beginning of the cytostoma, where a short, undulating membrane may also be seen. These parasites are provided with a trophonucleus and a kinetonucleus, and during their life history they undergo encystment, this probably representing the infective stage of the organism. Only one species, *T. mesnili*, is known to be parasite of the intestine of man.

Tetramitus Mesnili (Wenyon, 1910).—This parasite is found in the intestine of man. It is about the same size as *Trichomonas intestinalis*, with which it is often confounded. When seen alive, and in fresh preparations, the parasite is very active and almost indistinguishable from *Trichomonas intestinalis*. The fact, however, that the tetramitus is provided with a cytostoma, which may be seen in the stained preparation, is a valuable point in the differentiation. In addition, the trophonucleus and the kinetonucleus are situated more anteriorly and closer together than in *T. intestinalis*. The encysted forms, about 5μ in length are usually abundant in *T. mesnili*.

The pathogenesis of *T. mesnili* is not well understood. The parasite may be associated with other protozoan parasites, such as amebas.

It has been demonstrated that the presence of *T. mesnili* in the intestine is accompanied by a diminution or an absence of hydrochloric

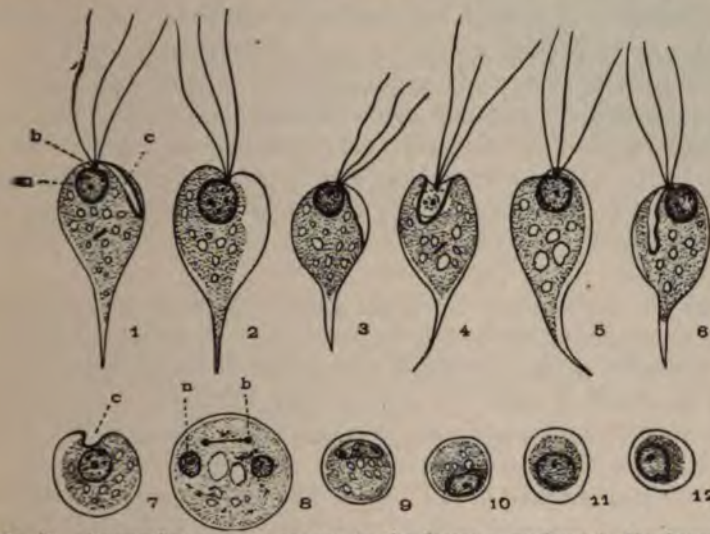


FIG. 71.—Tetramitus mesnili as seen in the feces; *n*, nucleus; *b*, blephoroplast; *c*, cystostoma; 1 to 7, several aspects of the parasite; division form; 9 to 12, encysted forms (*Iron hematoxylin stain from a case of Drs. Mathieu et Croiffou after Brumpt.*)

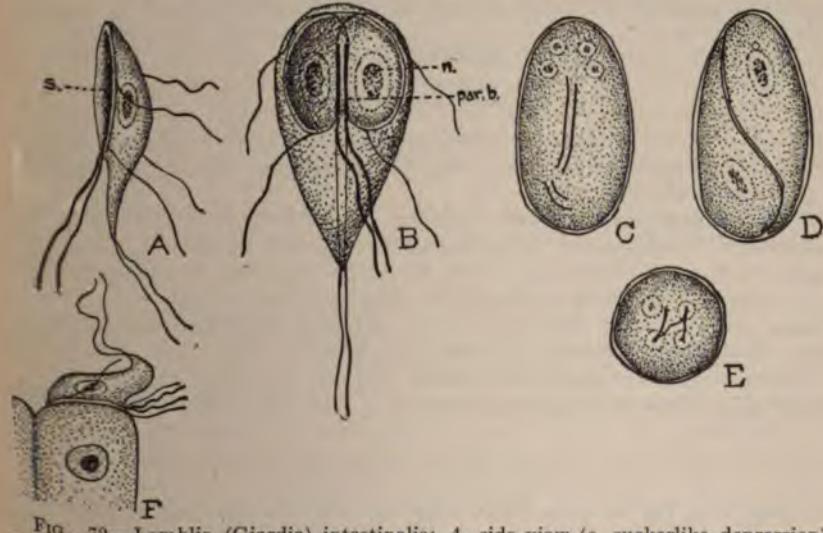


FIG. 72.—Lamblia (Giardia) intestinalis: *A*, side view (*s.* suckerlike depression); *B*, Ventral view (*par.b*, parabasal bodies, *n*, nucleus). *C*, young cyst with four nuclei; *D*, mature cyst containing two parasites; *E*, end view of young cyst; *F*, parasite resting on epithelial cell. (*A–E* × 2000 *after Wenyon; F* × 1000 *after Grassi and Schemiakoff*, in Chandler.)

acid in the stomach, a finding that, however, obtains also in the majority of cases of protozoan infection of the intestine.

IV. FAMILY LAMBLIAIDÆ (Blanchard, 1888)

The *Lambliaidæ* are pear-shaped, flagellated protozoa, characterized by the presence of a large depression or cytostoma in the anterior half of the body, around which two pairs of flagella are given off—one from the anterior and one from the posterior part of the cavity. An additional pair of flagella are given off from the posterior part of the body, making six flagella in all. An extra pair of flagella has been observed. In stained preparations two trophonuclei and three kinetonuclei are seen, on which the six flagella are inserted, one for each pair. One species, *L. intestinalis*, is known to be a parasite of the intestine of man.

Lamblia intestinalis (Lambl, 1859).—This is a pear-shaped flagellate, measuring 10 to 20μ by 6 to 10μ. It is commonly found in the intestine of rats and mice, and is also occasionally seen in the normal intestine of man. It is more apt, however, to be found in cases of diarrhea and amebiasis. Multiplication takes place by fission, and in cases of diarrhea encysted forms, measuring 10 to 13μ by 8 to 9μ, are commonly found in the feces. The pathogenesis is not clearly understood, but it seems certain that, like other intestinal protozoa, a previous alteration in the chemical constituents of the digestive tract is essential for Lamblia to thrive in this locality. Infection probably takes place through contaminated water or food.

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arasite in man). The evolutional forms of the malarial parasite and f other blood parasites are found in the mosquito and in other insects.

Life History.—The *Sporozoa* show the most complicated life histories of any of the protozoa. Alternation of generation is common. sexual reproduction, or *schizogony*, takes place by spore formation, nd sexual reproduction, or *sporogony*, is effected by the conjugation of he sexually differentiated gametocyte (male and female), formation f the *oökinet* and its subsequent development and cyclic evolution nto *oöcyte*, *sporoblast*, and *sporozoites* respectively. This sexual evolution may take place in the same host (*Coccidia*) or in an intermediate host, usually an insect (*plasmodium*). The sporozoites on being introduced into a susceptible host, become intracellular, grow into trophozoites, and the cycle is repeated.

Mechanism of Infection.—The infective stage in the cyclic evolution of *Sporozoa* is manifested by the sporozoites. These sporozoites, when formed in the same host as in *Coccidia*, are discharged with the feces, encysted and inclosed in a protective capsule. Infection takes place through the medium of water or food contaminated with these cysts, which reach the intestinal tract, where the capsule is digested and the sporozoites are set free to enter the epithelial cells and undergo multiplication, so that the cycle is repeated.

If the sporozoites are formed in an intermediate host, the mosquito, for example, as occurs in malarial fever, infection occurs as the result of the introduction of these sporozoites by the bite of the insect. The parasite becomes intracellular and undergoes multiplication and cyclic evolution. The mode of infection of *Sarcosporidia* and *Rhinosporidia* is not clearly understood. It is probable that in *Sarcosporidia* transmission takes place through the digestive tract (Theobald Smith) and that the *Rhinosporidia* are transmitted directly by contact.

Classification.—According to Schaudinn, the *Sporozoa* are divided into two classes: *Telosporidia* and *Neosporidia*.

Telosporidia.—These parasites are plasmodromatous protozoa, in which sporulation is distinct and separate from, and takes place at the end of the trophic phase of the parasite, as, for example, in the case of the malarial parasite. The *Telosporidia* are divided into the following groups: (I) *Gregarines;* (II) *Coccidia;* (III) *Hemosporidia.*

I. **Gregarines.**—These are parasites of the invertebrates, especially the Arthropods, in which they are abundantly present. It is characteristic of this group that only the young stage of the trophozoite is intracellular, whereas the fully grown forms are invariably found to be extracellular. These parasites usually inhabit the intestine, and apparently seem to be harmless to the host.

Morphologically, the gregarines vary in shape and size, some forms being only a few micra long, whereas others are relatively large, and

may be several millimeters long and readily visible to the naked eye They are gray, yellowish, or brown in color. A fully grown and typical gregarine appears as an elongated or bottle-shaped body, which is divided into two or three parts, named respectively *epimerite*, *protomerite*, and *deutomerite*. The deutomerite is the portion that contains the nucleus. Its cytoplasm is differentiated into ectoplasm and endoplasm. Vacuoles are absent or invisible. The parasites are deprived of cytoplasmic appendages for locomotion, and hence motility is very sluggish. Reproduction usually takes place by isogamy or anisogamy and encystment, with the formation of a single spore or cyst containing several sporozoites. Asexual reproduction does not, as a rule, occur. According to Leger, the gregarines are divided into—(1) *Eugregarines;* (2) *Schizogregarines*, and (3) *Aggregataria.*

1. *Eugregarines.*—The eugregarines are typical gregarines, and are commonly found in the intestine of invertebrates, especially in the arthropods. They are usually extracellular in nature. Reproduction takes place by isogamy or anisogamy, and consists of encystment, conjugation, and, with few exceptions, the formation of eight sporozoites. Asexual reproduction (schizogony) is unknown.

2. *Schizogregarines.*—Like the eugregarines, the schizogregarines are parasites inhabiting the intestines of invertebrates, arthropods, annelides, and tunicates, but they may also invade the Malpighian tubes and the connective tissue. Morphologically they resemble the eugregarines, from which they are differentiated chiefly by the occurrence of an asexual reproduction, which takes place during the early cytozoic (intracellular) stage. In the typical forms, however, the whole life is an extracellular one. Sexual reproduction, schizogamy, takes place by isogamy or anisogamy, as described for the eugregarines.

3. *Aggregataria.*—The aggregataria, often classed with the *Coccidia*, are parasites inhabiting the intestines of invertebrates (*Crustacea*) and vertebrates (fish). In some respects they resemble eugregarines, whereas in others they resemble *Coccidia*, to which they are closely allied. Asexual reproduction takes place in a crustacean (the crab), but these organisms are differentiated from all gregarines by the sexual reproduction that takes place by the conjugation of two differentiated gametes—a male and a female—without previous encystment of the individual gametes. For their life history the aggregataria require two hosts: a crustacean (the crab) in the intestine of which the trophozoite undergoes asexual reproduction, and a fish, in the intestine of which sexual reproduction takes place when the fish swallows the crab. Conjugation is accomplished by the union of the male and female gametocytes (microgamete formation has not been observed). The zygote gives rise to from 3 to 24 sporozoites.

II. **Coccidia.**—The *Coccidia* are parasites infesting invertebrates and the higher animals and man. They are intracellular in habit, and are found in the epithelial cells of the bile-ducts and intestine. Morphologically they are characterized by the fact that they have a distinct and constant shape, which is either oval or fusiform. Reproduction takes place by schizogony, with the formation, inside of the host cell, of several merozoites, and by sporogony, with the formation of a cyst or oöcyte containing a variable number of sporozoites. To fulfil their complete life history the *Coccidia* require only one host. Leger divides the *Coccidia* into four families, according to the number of sporozoites in the cyst:

Family 1: *Asporocystidæ:* sporozoite naked; no sporocysts inside the oöcyst.

Family 2: *Disporocystidæ:* oöcyst with two spores.

Family 3: *Tetrasporocystidæ:* oöcyst with four spores.

Family 4: *Polysporocystidæ:* oöcyst with many spores.

III. **Hemosporidia.**—The Hemosporidia are blood parasites of animals and of man. They are intracellular in habit, and are found in the blood either in the leukocytes (leukocytozoa or leukocytogregarines) or in the erythrocytes (malarial parasite) and hemogregarines. The hemosporidia usually require two hosts to complete their life history.

Neosporidia.—The *Neosporidia* constitute a distinct group of parasitic plasmodromata which probably have no relation to the *Telosporidia* (Döflein). As has been stated, in *Telosporidia* sporulation takes place at the end of the trophic phase of the parasite; that is, the trophozoite grows into a schizont and then divides into spores or merozoites (*e.g.*, hematozoa of malaria); in the *Neosporidia*, on the other hand, with few exceptions, growth and sporulation proceed together and simultaneously. In this respect it would seem that the *Neosporidia* are more closely related to the Rhizopoda than to the *Telosporidia*, and since most of their life is extracellular, the *Neosporidia* may be said to represent a lower degree of parasitic evolution. The *Neosporidia* are parasites of the lower animals and of man, and inhabit the epithelium of the intestine, bile-duct, connective tissue, and muscle. They are divided into four families: (1) *Myxosporidiæ;* (2) *Actomyxidiæ;* (3) *Sarcosporidiæ*, and (4) *Haplosporidiæ.*

1. *Myxosporidiæ.*—This family is characterized by the presence of an ameboid trophozoite. Sporulation begins early, during the trophic phase of the parasite. The spores formed may number two or more, and are provided with one or more polar capsules. These *Sporozoa* are usually found in fish, amphibia, and reptiles. Those that are found in fish have long been known as *Psorosperms*, and are known to inhabit the bile-passages, urinary organs, muscles, etc.

2. *Actinomyxidia.*—In the *Actinomyxidia* only the sporulation form is known. These *Sporozoa* are found in the annelides. The adult parasite appears as a pansporoblastic mass, inclosed in a capsule containing the spores; in this respect they resemble Sarcocystis, except that in the *Actinomyxidia* the number of spores is smaller—*i.e.*, about eight—and they are provided with polar capsules.

3. *Sarcosporidiæ.*—Our knowledge regarding the *Sarcosporidia* is very meager. The trophozoite appears as a round, oval, or elongated pansporoblastic mass between the muscle-fibers, surrounded by a double capsule inclosing numerous spores. Spore formation commences early and proceeds during the whole growth of the trophozoite, which may attain a very large size (16 to 50 mm. in length). The earlier life is intracellular in the muscle-cells, where it appears as an ameboid-like form (Erdmann) provided with two nuclei. Multiplication and growth give rise to sporoblast formation several being formed, and each one giving off several spores. According to Negri and Erdmann, the sporoblasts further multiply by division during sporulation, so that while development of the spores has begun at the center of the pansporoblastic mass, growth continues at the periphery or poles of the mass or trophozoite. The spores are oval, elongated, or banana-shaped bodies having no polar capsule. The *Sarcosporidia* are parasites of the higher animals and of man, and are found between the muscle-fibers. One form especially, *Sarcocystis tenella*, is common in the tropics.

Haplosporidiæ.—The *Haplosporidia* are closely allied to the *Myxosporidia*, from which they are differentiated by the absence of a polar capsule in the spore. These parasites are very simple in structure, and inhabit the tissues of invertebrates. They have been found in tumors of fish, and one species (*Rhinosporidium seeberi*) is found in man. The life history apparently is very simple. Asexual reproduction takes place in the following manner: On entering the host the young trophozoite becomes encysted, multiplies, and gives rise to a multinucleated mass of cytoplasm that divides, forming several sporoblasts (pansporoblasts) containing the merozoites or spores. When the cyst ruptures, these spores are set free, invade the surrounding tissue, grow into trophozoites, and the cycle is repeated. Sexual reproduction is not known.

For convenience of study the parasitic *Sporozoa* in man may be arranged in the following order:

I. Coccidia.
   (1) *Coccidium cuniculi.*
   (2) *Coccidium hominis.*
   (3) *Coccidium bigemini.*
   (4) *Eimeria hominis.*

II. Hemosporidia.
- (1) *Plasmodium malariæ* (quartan parasite).
- (2) *Plasmodium vivax* (tertian parasite).
- (3) *Plasmodium falciparum* (subtertian parasite).

III. Sarcosporidia.
- (1) *Sarcocystis tenella.*
- (2) *Sarcocystis muris.*
- (3) *Sarcocystis mucosa.*

IV. Haplosporidia.
- *Rhinosporidia seeberi.*

Pathogenesis.—Among the *Sporozoa* some species are found that are the cause of important diseases in man. The *Hemosporidia* alone are probably responsible directly or indirectly for at least one-third of the diseases common to man in the tropical countries. The *Coccidia*, *Sarcosporidia*, and *Haplosporidia* are less important.

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CHAPTER VIII

SPOROZOA (Continued)

THE PARASITIC SPOROZOA OF MAN

I. *Coccidia.*—II. *Hemosporidia.*—III. *Sarcosporidia.*—IV.

Haplosporidia.

I. THE COCCIDIA

History.—Habitat.—Animal Inoculation.—Cultures.—Life History.—Mechanism of Infection.—Pathogenesis.—*Coccidium cuniculi.*—*C. hominis.*—*C. bigemini.*—*Eimeria hominis.*

The Coccidia are telosporidial Sporozoa, usually found in the epithelial cells. Reproduction takes place both asexually (schizogony) and sexually (sporogony). Inside the cell the young parasites appear as small, oval, ameboid or round bodies, provided with a single nucleus. Sporulation takes place with the formation of numerous merozoites, or spores that are elongated or fusiform in shape. Encysted forms undergoing sexual reproduction may also be seen, which eventually lead to the formation of sporozoites.

History.—The Coccidia were first recognized by Hake in 1839. In 1845 Remak discovered the animal nature of these parasites, and in 1854 Lieberkühn showed that they were allied to gregarines. Leuckart, in 1876, gave the parasite the name *Coccidium*. In 1900 Schaudinn first described the complete life history of *Coccidium schubergi*, a parasite found in the epithelial cells of the intestine of the centipede (*Lithobius forficatus*).

Habitat.—The Coccidia are parasites of invertebrate and vertebrate animals. They are found most frequently in the lower animals as in rabbits, dogs, etc., and occasionally in man, inhabiting the epithelial cells of the intestine and also of the gall-bladder and bile-ducts.

Animal Inoculation.—Railliet and Lucet have succeeded in infecting rabbits with *Coccidium hominis*. Similar results can easily be obtained with *C. cuniculi* by having the animal swallow oöcysts containing sporozoites. Man is infected in a similar manner.

Cultures.—Artificial cultures of the Coccidia *in vitro* have not been obtained.

Life History.—Reproduction of Coccidia takes place asexually and sexually. The complete life history of these parasites, as first

escribed by Schaudinn from his observations on *C. schubergi*, is s follows:

Asexual Reproduction.—Asexual reproduction, also called schizo-ony, begins with the penetration of the sporozoites into the epithelial ells of the intestine of the centipede (*Lithobius forficatus*). Within ne cell the young trophozoite becomes oval or round in shape, and rows very rapidly at the expense of the protoplasm of the host cell. t attains full size and becomes a schizont in about twenty-four hours.



FIG. 73.—Life cycle of Coccidium schubergi. (*After Schaudinn.*) Sporozoites penetrate epithelial cells, and grow into adult intracellular parasites (*a*). When mature, the nucleus divides repeatedly (*b*), and each of its subdivisions becomes the nucleus of a merozoite (*c*). These enter new epithelial cells, and the cycle is repeated many times. After five or six days of incubation, the merozoites develop into sexually differentiated gametes; some are large and well stored with yolk material (*d, e, f*); others have nuclei which fragment into many smaller particles ("Chromidien"), each granule becoming the nucleus of a microgamete or male cell (*d*), (*hij*). The macrogamete is fertilized by one microgamete (*g*), and the copula immediately secretes a fertilization membrane which hardens into a cyst. The cleavage nucleus divides twice, and each of the four daughter nuclei forms a sporoblast (*k*) in which two sporozoites are produced (*l*). (*In Calkins.*)

The nucleus of the full-grown schizont, divides into daughter nuclei, and by a process of spore formation a number of merozoites are formed. The host cell, which from the beginning has undergone degeneration, is gradually absorbed and destroyed, and on being set free by the breaking up of the schizont the merozoite reënters a new cell and the cycle is repeated, thus augmenting infection of the host.

Sexual Reproduction.—As asexual reproduction does not go on indefinitely, when the environmental condition is unfavorable or because of a peculiarity in the life cycle of the parasite, sexual reproduction, or *sporogony*, occurs in the following manner: On entering the cell some of the merozoites grow and become differentiated into *microgametocytes* (male elements) and others into *macrogametocytes* (female elements). The microgametocyte is recognized as a round body inside of the host cell, and is provided with a finely granular protoplasm, which is poor in reserve material, and a fairly large nucleus, which is rich in chromatin. The macrogametocyte appears as an oval or bean-shaped body; its cytoplasm is rich in reserve material, and the nucleus is relatively small and poor in chromatin.

The microgametocyte leaves the host cell and gives off several microgametes or spermatozoites. At the onset of this process the nucleus becoming irregular, and this is followed by fragmentation into chromidia. The chromidia travel toward the periphery and become aggregated into several chromidial patches. Fusion of these patches into chromatin masses next takes place, and these, becoming lengthened, eventually project from the cytoplasm in the form of flagella. Finally the microgamete or spermatozoite is set free and becomes actively motile.

By the expulsion of the karyosome of the nucleus (polar body) the macrogametocyte develops into a mature macrogamete, and in this stage leaves the host cell.

Conjugation now takes place by the fusion of microgametocyte and macrogametocyte and the formation of a *synkaryon* or *zygote*, which becomes surrounded by a protective membrane and constitutes the *oöcyst*. In this stage it passes out of the body of the host in the encysted form and divides into four sporoblasts. Each of these sporoblasts develops a cyst wall and becomes a "spore," which, by division of the nucleus finally gives rise to eight sporozoites. On being swallowed by a susceptible host and reaching the stomach, the capsule of the cyst is dissolved, and the sporozoites, being set free, enter the epithelial cells of the intestine and repeat the cycle.

Sporogony is completed in from two to three days, and takes place only outside of the host or in the cadaver, as the body temperature or the chemical processes of the intestine during life seem to be unfavorable for its development.

Mechanism of Infection.—The infective stage in the life history of the Coccidia is represented by the encysted sporozoites. Infection takes place through the medium of infected food or contaminated water. On reaching the stomach and the intestine the cyst ruptures, the sporozoites are set free, and enter the epithelial cells as young trophozoites. The parasite now grows and becomes a schizont; multipli-

cation takes place, and the merozoites, being set free by the rupturing of the schizont, enter new cells.

Pathogenesis.—Although commonly found in the lower animals, especially in rabbits, the Coccidia are occasionally parasites of man. Coccidial infection of man manifests itself by gastroenteric and hepatic disturbances. Three species of Coccidia have been found to be parasitic in man: (1) *Coccidium cuniculi;* (2) *C. hominis;* (3) *C. bigemini.* One other species, *Eimeria hominis,* has been reported by Künstler and Pitres. Several observers have regarded as Coccidia mere protoplasmic inclusions or the yeast-like fungus cells that are commonly found in cancer.

1. **Coccidium cuniculi** (Rivolta, 1878).—The young trophozoite measures from 9 to 10μ. The oöcysts are ovoid in shape, from 30 to 49μ by 28μ, and contain four spores, each of which contains two sporozoites.

Habitat.—The parasite is commonly found in rabbits. It most frequently invades the epithelium of the bile-ducts, but it may also infest that of the intestine. It is readily demonstrated in the feces of an infested rabbit, and also in the intestine and mesenteric ganglion. Occasionally it may be also found in the biliary passages of man.

Animal Inoculation.—Young rabbits can be infested experimentally by the ingestion of cultures of oöcysts obtained from the liver of a parasitized rabbit (Lucet).

Life History.—The life history of this parasite is identical with that of *C. schubergi* described above. Reproduction takes place asexually with the formation of merozoites, and sexually with the production of sporozoites.

Mechanism of Infection.—The infective stage in the life cycle of the parasite is represented by the sporozoites contained within the oöcyte. Rabbits and men are infected through the medium of contaminated food or water.

Pathogenesis.—In man and in rabbits the seat of infection is in the bile-passages. The condition manifests itself by hepatic and intestinal disturbances.

2. **Coccidium hominis** (Rivolta, 1878).—This parasite is frequently found in the feces of rabbits. It inhabits the epithelium of the villi of the intestine and appendix. In a few instances it has been found in man. It closely resembles *C. cuniculi,* with which it may be identical, the chief difference consisting in the size of the oöcyst, which is said to be smaller in *C. hominis* (25 to 35μ) than in *C. cuniculi.* Another point in the differentiation between the two parasites is that *C. hominis* usually inhabits the intestine, whereas *C. cuniculi* is commonly found in the bile-ducts.

The life cycle and mode of transmission of the parasite are identical with those of *C. cuniculi.*

3. **Coccidium bigemini** (Stiles, 1891).—The parasite is found abundantly in dogs and in cats, but is only occasionally seen in man. It inhabits the villi, and not the epithelium, of the intestine. The oöcysts of this coccidium are formed in the intestine of the host.

4. **Eimeria hominis** (Blanchard, 1895).—Künstler and Pitres have described oval-shaped, oöcyst-like bodies in the purulent material taken from the pleura of a case of chronic pleurisy. The exact habitat of the parasite has not been determined. It was regarded as a coccidium because of the fact that numerous sporozoites were found within the bodies.

II. THE HEMOSPORIDIA

History.—Habitat.—Animal Inoculation.—Immunity.—Cultures.—Life History.—Mechanism of Infection.—Pathogenesis.—*Plasmodium vivax.*—*Plasmodium malariæ*—*P. falciparum.*—Hemosporidia of the Lower Animals: Genus Hemoproteus; Lankesterella; Leukocytozoa; Babesia; Hemogregarina.

The Hemosporidia are telosporidian Sporozoa existing as parasites in the cellular elements of the blood of vertebrates. The forms found in the blood of man are commonly known as *Plasmodia* (Laveran); they inhabit the erythrocytes, and the trophozoitic phase of the parasite is always ameboid. A characteristic of these Sporozoa is that a pigment, called *hemozoin,* is present in the protoplasm; this is derived from the hemoglobin of the parasitized erythrocyte, and represents the excrementitious products of the organisms.

Except in very young or ring forms, and in the adult stage (schizont), the trophozoite is extremely dysmorphic and ameba-like in form. Reproduction takes place asexually inside of the body in the erythrocyte, and sexually outside of the body in an intermediate host. The sexually differentiated forms (gametocytes) are usually globular or crescent like in shape. At no stage of development in the life history are the *Hemosporidia* provided with a well-developed and permanent flagellum.

History.—The malarial parasite was discovered by Laveran on November 6, 1880. Markel in 1874, and Virchow in 1848, had previously observed pigmented protoplasmic masses in the blood of man; these they described as "pigmented leukocytes," asserting that they were pathognomonic of malarial infection. These pigmented protoplasmic masses were in reality malarial parasites, but these observers failed to recognize their parasitic nature. We owe our present knowledge of this parasite largely to the researches of Laveran, Golgi, Marchiafava, Celli, Bignami, Bastianelli, and others, but more especially to Golgi, who discovered the plurality of the malarial parasite.

Manson advanced the theory of the possible transmission of malarial fever by mosquitos, and working on this theory Ross traced the development of the malarial parasite of birds (Proteosoma) to *Culex* and Grassi traced the development of the malarial parasite in man to *Anopheles*. Manson finally showed that the transmission of malarial fever occurred through the bite of an infected *Anopheles*.

Habitat.—The *Hemosporidia* inhabit the cellular elements of the blood. Several species are known at the present time, and their number is still being augmented. Almost every known vertebrate has been found to serve as a host of one or another variety of these parasites. Most of the species are so closely allied, however, that they cannot be differentiated morphologically. The malarial parasite of man and that of the monkey, for example, can be differentiated only as the result of crossed inoculation. Man is immune to malarial fever of monkeys and *vice versa*.

Animal Inoculation.—The malarial parasites are peculiar in that they are inoculable only in animals of the same species. Thus man can be infected only by the injection of parasitized blood from another man, but not from that of any of the lower animals. Similarly the malarial parasite of monkeys or of any of the other lower animals is inoculable only for homologous species.

Immunity.—There is no evidence to show with certainty that one attack of malarial fever confers immunity against a second infection. On the contrary, man seems to be susceptible to reinfection. Koch showed the preponderance of malarial infection among the native children of Africa from the first to the fifth year, as compared with adults in the same locality, and suggested the possibility of a certain degree of acquired immunity during childhood. Although this may be possible, the relative infrequency of malarial fever among adults is more likely following the law of "survival of the fittest," or a natural resistance to infection rather than to an actual immunity. It may also be added that malarial fever, like tuberculosis, is common to all ages, although both diseases are more prevalent in childhood and in early life. This may be explained by the fact that, all things being equal, besides the strength of the virus, the quantity—that is, the amount inoculated—has an important bearing upon the infection. It is reasonable to suppose that while the number of sporozoites injected by a single bite of a mosquito, may be incapable of producing infection in an adult of average weight (140 pounds), the same number of sporozoites may easily cause infection in a child.

Cultures.—Bass has succeeded in obtaining cultures *in vitro* of the malarial parasite. He used sterile defibrinated blood to which 0.1 c.c. of a 50 per cent. sterile dextrose solution was added for each 10 c.c. of blood (0.5 per cent. dextrose). For successful cultivation the follow-

ing precautions are recommended by Bass. (1) Avoid bubbles and unnecessary exposure to the air of the blood during defibrination; (2) avoid, as much as possible, the presence of leukocytes in the medium; (3) the column of blood should be 1.5 to 5 cm. deep, and the column of serum 1.2 to 2.5 cm.; (4) culture tubes with flat bottoms are preferable, and they should not be less than 1.2 cm. in diameter; (5) the cultures should be free from bacterial contamination; (6) the tubes should be disturbed as little as possible during inoculation and in subsequent manipulations for examination. The technic is as follows:

Ten cubic centimeters of parasitized blood are collected from the vein of the forearm with the aid of a syringe and expelled directly into a sterile test-tube containing 0.1 of a 50 per cent. sterile dextrose solution. The tube is provided with a glass rod for defibrination of the blood. The blood is defibrinated, incubated at 38° to 40° C., and examined at regular intervals. This procedure will suffice for the growth of only one generation of the parasites. If the blood is collected during the febrile stage, for example, in a case of tertian infection, when the parasite is in the ring form, the trophozoite will be seen to grow gradually to a schizont and to undergo segmentation in about forty-eight hours. Specimens for examination are collected with the aid of a pipet. The parasite grows only at the top of the column in a layer varying in thickness from 0.05 to 0.1 cm. All the parasites beneath this layer perish.

For the cultivation of more than one generation the parasitized blood is defibrinated and centrifugalized. Specimens of blood are collected with the aid of a pipet and inoculated into freshly prepared culture-tubes containing fresh leukocyte-free defibrinated blood to which the proper amount of leukocyte-free serum and dextrose have been added. The tubes are then incubated at 38° to 40° C. The parasites develop in this leukocyte-free culture, they undergo segmentation, and on being set free the merozoites enter new erythrocytes. On subsequent transplantations fewer parasites survive (actually, out of from 15 to 30 parasites, only one survives), and finally the culture is dissipated. Bass has succeeded in obtaining as many as three, and with a more rigorous technic even a fifth generation was cultivated, but the culture could not be continued indefinitely.

Life History.—The life history of *Hemosporidia* is a very complicated one. Alternation of generation is the rule. Asexual and sexual reproduction take place in much the same way as in the Coccidia, except that while in Coccidia sexual reproduction usually begins in the same host and is completed outside, sexual reproduction of the *Hemosporidia*, as, *e.g.*, *Malarial parasite* (Fig. 74 and Plate VI), takes place through an intermediate host—the mosquito.

Asexual Reproduction.—The asexual reproduction or schizogony

of *Hemosporidia* is almost identical with the asexual reproduction in Coccidia, except that in the former the process takes place in the erythrocyte or leukocyte, whereas in the latter it occurs in the epithelial cells of the intestine or bile-duct. The malarial parasite is found in the salivary gland of an infected mosquito of the family *Anophelinæ*.



FIG. 74.—Diagram of the Life-Cycle of Plasmodium vivax.

1, Sporozoite entering red cell; 2, trophozoite; 3–4, schizont; 5, merozoites; 6, merozoites entering red cell; 7, young trophozoite; 8*a*–10*a*, development of a microgametocyte; 8*b*–10*b*, development of a macrogametocyte; 10*b*–10*e*, parthenogenesis; 11*a*–12*a*, formation of a microgamete; 11*b*–12*b*, formation of a macrogamete; 13, zygosis; 14, oökinete; 15, oöcyst; 16, formation of sporoblasts; 17, formation of sporozoites; 18, cyst ruptured and sporozoites escaping; 19*a*, sporozoites infecting the ovary; 19*b*, sporozoites infecting the salivary glands; 21, sporozoites escaping from the salivary duct and entering the human skin; 22, this indicates that the further development of the sporozoites infecting the ovary is unknown. (*After Castellani and Chalmers.*)

It is a fusiform body, 10 to 20μ by 1 to 2μ in size, and is known as a *sporozoite*. It consists of a cytoplasm containing a nucleus rich in chromatin. The infection is transmitted to man through the bite of an infected mosquito, and on entering the body, the sporozoite penetrates the erythrocyte and becomes an intracorpuscular trophozoite.

Shortly after entering an erythrocyte the young trophozoite appears as a small round and refracting body, from 1.5 to 3 μ in length, some-

what clear at the center because of the presence of a vacuole, which, when stained, gives to the young parasite the characteristic *ring-like* appearance. At this stage the parasite is made up of a small protoplasmic mass, condensed at the periphery into the form of a ring, thick at one side and delicate and thin at the other, inclosing a well-formed vacuole in its center. It contains a small and deeply stained nucleus, which is situated at the thinner part of the ring. Pigment is usually absent, or so small in quantity as to be invisible in the very young trophozoite, but becoming more marked in the larger ring forms.

As the trophozoite grows it becomes ameboid, the vacuole disappears, and the characteristic pigment, known as *hemozoin*, becomes visible in the form of small grains which are black or brownish red in color. This pigment is hemic in origin, and represents an excrementitious product of the parasite. In fresh preparations the parasite appears actively motile, the movements being vibratory, wave-like, or ameboid in nature, with pseudopod formation. The motility can best be seen by observing the movement of the pigment granules which follows the protoplasmic currents of the plasmodium.

As the parasite grows older it becomes sluggish; the ameboid shape is replaced by a more constant and definite form—usually oval or round; the outline is more distinct, and the pigment becomes more abundant. The full-grown *trophozoite* finally becomes rounded off; motility is nearly absent, it is full of pigment granules, and the nucleus is subcentrally located. This stage is called the *schizont*.

The schizont now begins to divide by a process of spore formation. The division is initiated by an accumulation of the pigment in some part of the cytoplasm, usually at the center, followed by mitotic division of the nucleus, so that from two to more than twenty nuclei may be seen. Each nucleus becomes surrounded with a mass of cytoplasm, and assumes the form of a *merozoite*. To the mass of merozoites within the erythrocytes the name roset, marguerite, or muriform bodies is commonly given.

A portion of the schizont containing the hemozoin, and known as the residual mass or *nucleus de relinquant*, is always left unsegmented.

The erythrocyte now breaks up, and the merozoites, residual protoplasm, and pigment are set free in the blood-stream, and although the pigment and some of the merozoites are taken up by the leukocytes and endothelial cells and destroyed, the greater number of the merozoites enter new erythrocytes and become trophozoites, and the cycle is repeated. Asexual reproduction takes place in from forty-eight to seventy-two hours, depending on the species of parasite.

Each sporozoite on entering an erythrocyte, gives rise to several merozoites, and as each of these again reproduce several merozoites, etc., the infection becomes gradually more severe, unless its course

is checked by phagocytosis, and more especially by quinin treatment. If the condition is not checked, in a certain number of days (from eight to twelve) the infection becomes more pronounced, manifesting itself in an attack of fever. This period of from eight to twelve days after the bite of the mosquito constitutes the incubation period.

Sexual Reproduction.—The sporozoite, as we have seen, develops directly into a schizont and for some time reproduces asexually forming merozoites: when, however, conditions become unfavorable for the parasite, or owing to peculiarities in the life cycle, these merozoites undergo differentiation into sexual forms, and some weeks after the attack of malarial fever (about three to four weeks after infection) sexual forms appear in the peripheral blood.

In the early stage the sexually differentiated parasite resembles a merozoite, and can be recognized only by the absence of vacuoles and by its growth, which is very slow. As it grows older and becomes more mature, the protoplasm of the female form, known as the *macrogametocyte*, becomes markedly granular and rich in pigment, whereas the male form, or *microgametocyte*, is less granular and poor in pigment. Three types of cells are, therefore, recognized in the malarial parasite, namely: the undifferentiated or *schizont*, the female and the male *gametocyte*.

The *macrogametocyte* is usually the larger, and possesses a small and eccentrically situated nucleus that is poor in chromatin. The cytoplasm is markedly granular and rich in pigment.

The *microgametocyte* is smaller than the male form, and the nucleus is large and rich in chromatin. The cytoplasm is clear and less markedly pigmented.

The macrogametocyte and the microgametocyte as found in the blood-stream are concerned with the sexual reproduction which takes place in the body of the female mosquito (the male does not suck blood).

If a female mosquito belonging to the family *Anophelinæ* (*Anopheles maculipennis*), sucks the blood of a person containing both the macrogametocytes and the microgametocytes, on reaching the stomach of the mosquito the macrogametocyte undergoes reduction by division of the nucleus (polar bodies). This reduced gametocyte is called a *macrogamete*. Similar changes take place in the microgametocyte: chromidial masses separate from the nucleus, travel to the periphery, and thin threads of protoplasm, from two to six in number, are formed from the body of the parasite, each being provided with a corresponding amount of chromatic substance; these finally break off and become free. The *microgamete* is actively motile, and is made up of a tapering thread of protoplasm and chromatin granules. It resembles a spirochete, but does not possess an undulating membrane.

Conjugation or *zygosis* now takes place, the male and female pronuclei fuse to form a *synkaryon* or *zygote*, which by virtue of its motility is called an *oökinete* or *vermicule*.

The oökinete penetrates the mucous membrane of the stomach of the mosquito, and on reaching the submucosa undergoes encystment. This stage is called the *oöcyst*. The oöcyst now grows rapidly, and the nucleus divides into a large number of daughter nuclei each surrounded by cytoplasm. At this stage the cell is called a *sporoblast*.

The nucleus of each sporoblast now divides into several small nuclei, which travel to the periphery, become surrounded by cytoplasm, and take on an elongated form. These fusiform bodies are termed *sporozoites*. Each sporoblast, therefore, gives rise to a great number of sporozoites. The cyst attains a large size, and can easily be seen under the low power of the microscope as a small, papillary-like projection on the surface of the stomach of the mosquito. In a fresh cover-glass preparation, under the high power of the microscope, the free sporozoites inside of the cyst are readily seen to be actively motile and moving in different directions.

The cyst finally ruptures and the sporozoites are set free in the celom of the insect. They are carried to all parts of its body, and finally find their way into the salivary gland and proboscis. With the bite of the mosquito the sporozoites are introduced into a new host; they enter the erythrocytes, become trophozoites, and the cycle is repeated. The sporozoites, by reaching the ovaries, may also infect the egg, and the infection may thus be carried to the next generation—a theory that has not been proved in fact.

With favorable temperature—20° to 30° C.—sporogony is complete in from about ten to twelve days. If the temperature is below 15° C. no development takes place and the parasite dies.

Mechanism of Infection.—As has been shown malarial infection is transmitted to man by means of the mosquito. It has also been seen that the infective stage in the life cycle of the parasite is represented by the sporozoites as found in the salivary gland or proboscis of the insect. Man is inoculated by the bite of an infected mosquito. Sargent observed the penetration of the sporozoite through the skin of birds by merely rubbing the surface of the thorax of an infected mosquito, and it is possible that this mode of infection may also take place in man.

How long these sporozoites can live and retain their virulence in the body of the mosquito is not known, but it is probably only for a short time—say a few weeks to two months. At any rate, it seems that the mosquito is infective only during one season.

In experimental work man may be infected by the injection of parasitized blood taken from another person suffering with acute

malarial fever. The fact that infected mosquitos have been found in places known to be uninhabited by man, as in some regions of Africa, has suggested the possibility that, besides man, some species of monkeys or of another higher vertebrate may serve as reservoirs for the virus. This suggestion has also been made for trypanosomes, but no definite knowledge upon these important questions exists. At present we know that the mosquito acts as the primary host of the parasite and that man is the secondary or intermediate host; that the mosquito becomes infected only after it sucks the blood of an infected person in which the gametocytes or sexually differentiated forms of the parasite are found, and that after a certain time (from ten to fifteen days), under favorable conditions, the virus is transmitted to man through the bite of the insect.

Pathogenesis.—The *hemosporidia* are the etiologic factors in a group of important diseases of man known as malarial infection or paludism. Three types of malarial fever are recognized: (1) Tertian; (2) quartan, and (3) subtertian; the last is also known as estivo-autumnal or tropical malaria. Each variety is produced by a different parasite, which is well differentiated morphologically and by its life cycle. Thus, the tertian parasite, the largest of the three, has an asexual cycle of forty-eight hours in the blood, and gives rise to from 12 to 20 merozoites; the quartan, which is intermediate in size between the other two, has an asexual cycle of seventy-two hours, and produces from 8 to 12 merozoites; the subtertian, the smallest of the three, has an asexual cycle of about forty-eight hours, and produces from 12 to 18 merozoites. In the subtertian variety the merozoites are very small, and the young trophozoite appears as a tiny ring measuring from 1 to 2μ in diameter. Furthermore, the gametocytes of the subtertian form are differentiated from the gametocytes of the tertian and the quartan forms by their characteristic crescentic shape.

1. **Plasmodium vivax** (Grassi and Feletti, 1890).—The *Plasmodium vivax* also called *Plasmodium malariæ, var. tertianæ*, is the cause of tertian malarial fever. It derives its name from the energetic ameboid movements of the trophozoite during its active growth. The parasite is markedly dysmorphic, and is characterized by its large size—it may be 8 or 9μ in diameter—by the fine character of the pigment present, and by the merozoites formed, these being larger and from 12 to 20μ in number. In the very young stage the ring form is relatively large; about one-third of the erythrocyte contains a large vacuole, and the nucleus or chromatic knob is placed in line with, and at the thinnest portion of, the ring. The appearance of the parasitized erythrocyte is characteristic; the cell, even from the beginning, is pale and edematous, and these features become more strongly accentuated as the parasite grows older (Plate VI). When stained with polychrome

stains, the corpuscular substance presents a dotted appearance, due to the presence of red granules, called *Schüffner's* dots.

Asexual Reproduction.—The process of schizogony of *P. vivax* is as follows: On entering the erythrocyte the sporozoite or merozoite remains in a quiescent stage for a certain length of time. In the case of a sporozoite this quiescent stage may be very short, but in the case of a merozoite it may last from four to eight hours or more, this time corresponding to the febrile period of the patient. The patient's temperature, ranging from 102° to 104° F. or more, is probably unfavorable to the growth and proper development of the young parasite. In either case the young trophozoite appears in the erythrocyte as a ring containing a relatively large vacuole. Within a few hours after the temperature has declined the parasite becomes ameboid and begins to grow very rapidly, so that within from twelve to thirty hours after the chill it reaches a fair size and occupies over two-thirds of the erythrocyte. At this stage the parasite is rich in pigment. After thirty hours it again becomes quiescent and globular in shape. In this stage it is called a *schizont*, and measures from 8.5 to 9μ in diameter.

After from thirty to forty-eight hours the fully grown schizont undergoes sporulation. The onset of the process is marked by an aggregation of the pigment, either toward the center or toward the periphery of the cytoplasm, and by division of the nucleus, so that after forty hours two, four, six, or more chromatin masses can easily be seen scattered in the protoplasm. After forty-eight hours from 12 to 20 merozoites are formed. At this stage the erythrocyte has become considerably edematous and almost colorless, and it finally ruptures, liberating the merozoites and the hemozoin. The pigment is taken up by the leukocytes and endothelial cells, the merozoites enter new erythrocytes, and the cycle is repeated. *P. vivax*, therefore, consumes forty-eight hours in the process of schizogony. The time of sporulation corresponds with the chill, and the time of invasion of new erythrocytes with the fever, whereas the quiescent or afebrile period corresponds with the growth of the parasite (Fig. 75 and Plate VI).

Sexual Reproduction.—The process of sporogony of *P. vivax* takes place in the mosquito, and was first worked out in *Anopheles claviger*. As described by Schaudinn; the development of the gametocytes, fertilization, and formation of the oökinete take place in the lumen of the stomach in about forty hours after feeding, and in about forty-eight hours the oökinete has become encysted (oöcyte). The oöcyte can be seen as a pigmented, round, and transparent body situated well beneath the epithelium, and surrounded by a distinct wall. At this stage the nucleus has begun to divide.

On the third day the oöcyte has increased in size, segmentation of the protoplasm around the nucleus takes place, and the formation

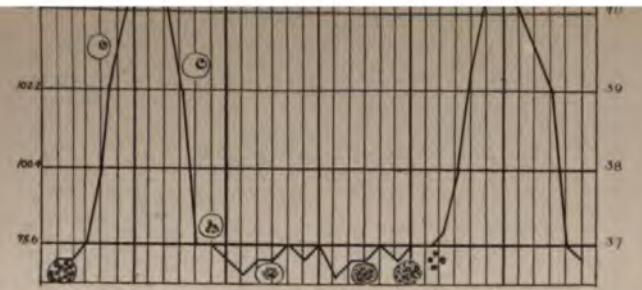
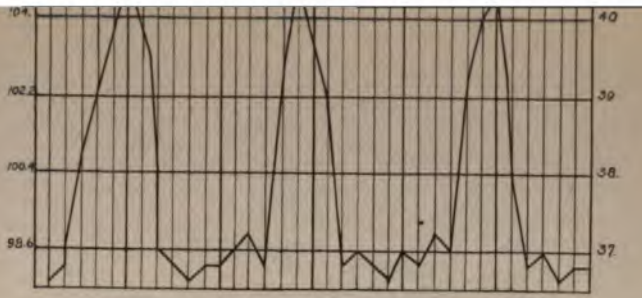
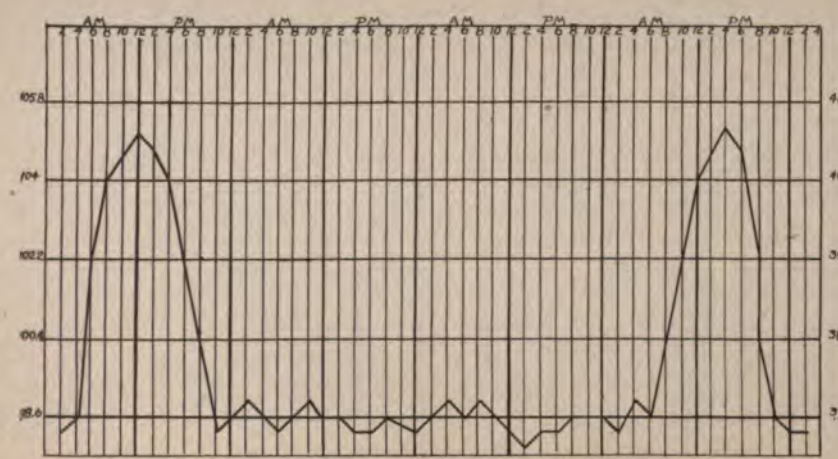


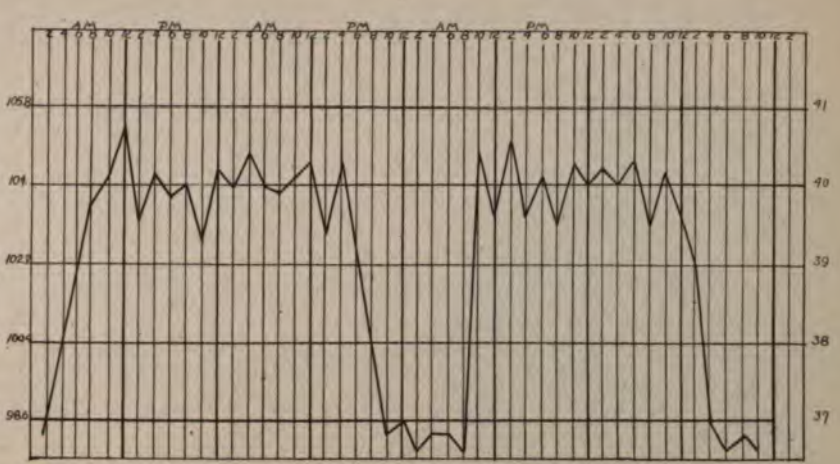
Chart of tertian malarial fever showing the different developmental forms of the malaria parasite in correspondence with the various periods of the attack.



Temperature chart of double tertian malaria.



Temperature chart of quartan malaria.



Temperature chart subtertian malaira.

FIG. 75.—Temperature charts of malarial fever.

of sporozoites has begun. This stage is called the *sporoblastic stage* or *sporoblast.*

During the fourth day the sporoblast has increased in size, and from 20 to 30 sporoblasts are formed, the periphery of which begins to be differentiated into developing *sporozoites.*

After the fifth day the cyst is about 59μ in diameter, projects into the celom, and contains numerous sporozoites. At this stage the cysts are easily recognizable under the low power of the microscope as small, papillary projections on the surface of the stomach, and if a cover-glass is applied, under the high power of the microscope the sporozoites may be seen as actively motile bodies, moving in all directions.

After the seventh day the cysts rupture, the sporozoites escape into the body cavity of the mosquito, and find their way to the salivary gland, where they occupy the cells, chiefly those of the middle or poison gland, and the proboscis. In from the tenth to the twelfth day the mosquito is capable of transmitting the virus to man through its bite. Thus the cycle of sporogony is completed. On reaching the circulation, the sporozoites enter the erythrocytes, become trophozoites, and the cycle is repeated.

Schaudinn observed the sporozoites in the ovary, and eventually in the eggs of the mosquito, but whether the virus is carried to the larva and to the pupa and thus into a second generation has not been determined.

Mechanism of Infection.—Malaria is a typical infectious disease, the virus being transmitted to man by the mosquito. The infective stage in the life cycle of the parasite is represented by the sporozoite, as found in the salivary gland and proboscis, and is introduced into man by the bite of the insect.

Pathogenesis.—*P. vivax,* or the tertian malarial parasite, as it is commonly called, is the cause of tertian malarial fever. The disease is characterized by a sudden attack of chills, followed by a high temperature—103° to 104° F.—which lasts from four to eight hours, when the fever subsides. The attack is repeated with some degree of regularity every forty-eight hours.

Cultures.—The parasite, as previously stated, has been artificially cultivated by Bass and grows in a dextrose blood medium.

2. **Plasmodium malariæ** (Laveran, 1881).—This plasmodium, also called *P. malariæ quartanæ,* is the parasite of quartan malarial fever in man. In all stages of its asexual development it is smaller than the tertian parasite. When full grown, it is about 6μ in diameter. During its growth the trophozoite is less active and less ameboid in shape than the tertian parasite, and the pigment is somewhat coarse. It is characteristic of the parasite that it appears as an equatorial

band in the cell and produces no appreciable changes in the size of the erythrocyte. When fully grown, the schizont is almost round in shape and regularly outlined. The number of merozoites produced are from 6 to 12 (Plate VI).

Asexual Reproduction.—The young trophozoite appears as a compact ring in the erythrocyte, somewhat smaller than the ring forms of *P. vivax*, the chromatin being inside of the ring. Growth is slow, and after twenty-four hours it has reached something over one-third of the erythrocyte. At this stage the pigment is distinct, coarse, and dark in color, and is not uncommonly aggregated at the periphery of the parasite. The parasitized erythrocyte, as has been stated, undergoes no appreciable change other than it may become darker and somewhat smaller.

After sixty hours have elapsed the parasite has become a full-grown schizont. It now appears as a round, pigmented body, surrounded by a rim of red blood-cells. At this time nuclear division takes place, the first manifestation being concentration of the pigment in some part of the cytoplasm, usually toward the center. Finally, after seventy-two hours, from 6 to 12 merozoites are formed.

The erythrocyte now breaks up, and the merozoites, which are about 1.7μ in length, are liberated; they enter a new cell, become trophozoites and the cycle is repeated. The whole process of schizogony occupies seventy-two hours (Plate VI).

Sexual Reproduction.—Sporogony takes place in *P. malaria* in the same manner as in *P. vivax*, previously described, except that it takes longer—from eighteen to twenty-one days being required for its completion.

The macrogametocyte, as found in the peripheral blood, can be recognized by the fact that it is a little larger than the erythrocyte (7 to 8μ). When stained, the cytoplasm is granular and darker than the cytoplasm of the schizonts, and appears to be surrounded by a very small rim of the corpuscle.

The microgametocyte is rich in chromatin, and smaller, as a rule, than the macrogametocyte. It is less pigmented, and its cytoplasm is clearer; the parasitized cell is not larger, and the corpuscular rim is more distinct.

The sexually differentiated parasites are found in the peripheral blood, but not before the third or fourth week after infection has occurred or after the second week of the first febrile attack. Differentiation of the sexual forms from the schizont is no easy matter, but the difficulty can be overcome, to a certain extent, by making a systematic study of the blood. We know that the chill corresponds in time of onset to that of sporulation of the parasite; that the period of fever, and for several hours after the temperature has subsided, corresponds

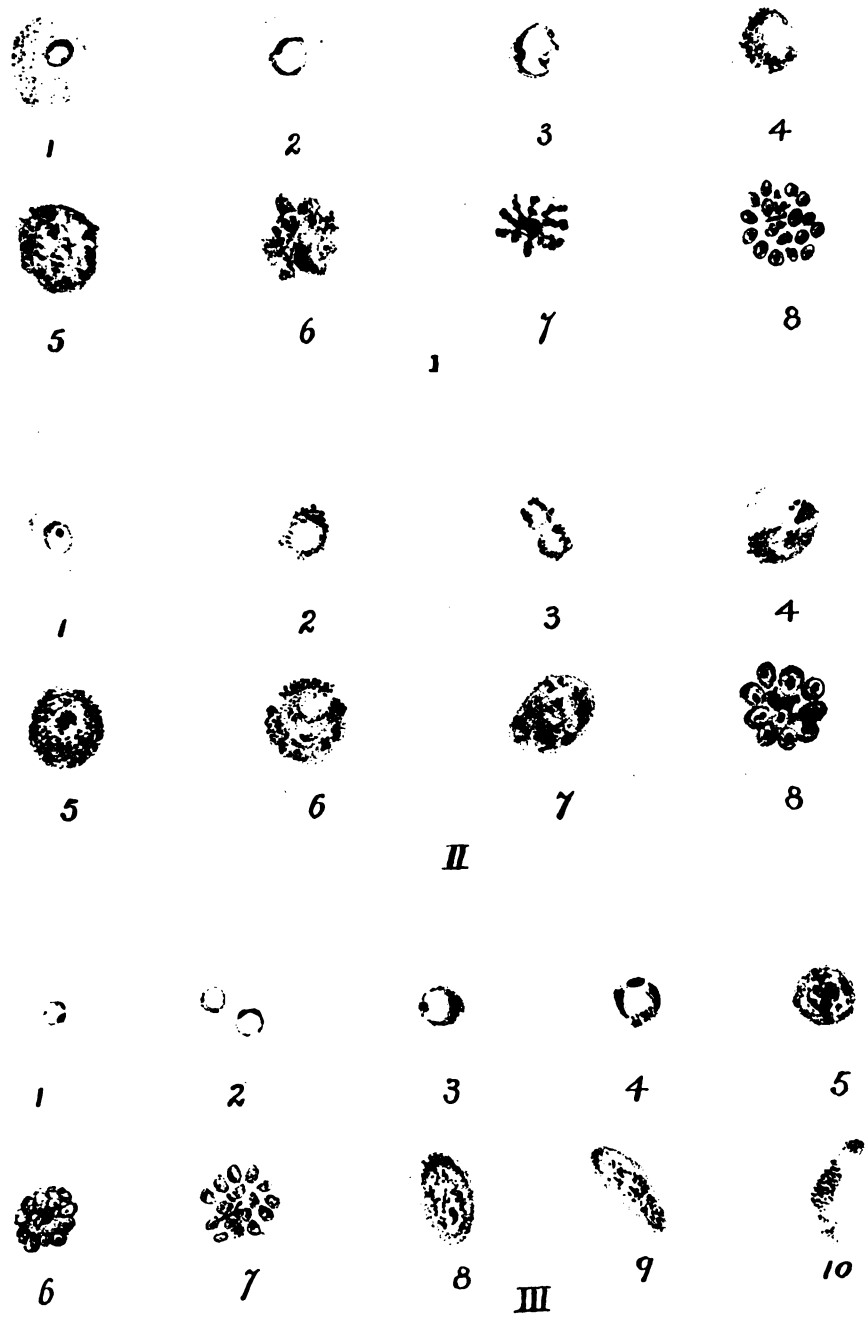


PLATE VI—Malaria parasite stained by diluted borax methylene-blue. I. Tertian parasite. 1, ring form; 2, 3, and 4, young trophozoites; 5, fully grown schizont; 6, schizont about to divide; 7, beginning sporulation; 8, sporulation form, the schizont divided into merozoites. II. Quartan parasite. 1, ring form; 2 and 3, young trophozoites; 4, half grown trophozoite; 5, fully grown schizont; 6, schizont about to divide; 7, beginning sporulation; 8, schizont divided into merozoites. III. Subtertian parasite. 1, ring form; 2, 3 and 4, different stages of a trophozoite; 5, schizont beginning sporulation; 6 and 7, sporulation forms, the schizont divided into merozoites; 8, 9 and 10, different types of a crescent-shaped form or gamete.

to the younger stage of the trophozoite, commonly known as the ring form, so that if the blood is examined at intervals during this time and the stained preparations constantly show full-grown forms, without any indication of nuclear division, these forms are in all probability gametocytes. This is true only if the infection is of one, two, or three weeks' standing, and if a double or triple infection can be eliminated. What has been said of the quartan parasite is applicable also to the tertian form.

It is essential that these factors be taken into consideration before attempting the experimental infection of mosquitos. If no gametocytes are present in the peripheral blood the result will be negative. This is true also in the study of flagellate forms *in vitro* in fresh cover-glass preparations under the microscope.

Mechanism of Infection.—The virus is inoculated into man by the bite of the mosquito, the infecting agent being the sporozoites as found in the salivary gland and proboscis of the insect.

Pathogenesis.—The quartan malarial parasite is the cause of quartan malarial fever in man. This disease, like tertian malarial fever, is characterized by chills and fever, which last from four to eight hours, but are followed by a period of exacerbation lasting two days instead of twenty-four hours, as is the case in the tertian affection, and the attack is repeated with considerable regularity every seventy-two hours. Quartan malarial fever is usually mild in character. A severe infection is the exception, and only in very few cases does it prove fatal (Leishmann).

Cultures.—Bass and Johns could not cultivate this parasite artificially.

3. **Plasmodium falciparum** (Welch, 1897).—*Plasmodium falciparum*, also called *P. precox*, *Laverania malariæ*, or *P. malariæ var. quotidianæ*, is the parasite of subtertian malarial fever, commonly known as estivoautumnal or tropical malaria. In the trophozoite stage, the parasite, as commonly seen in the peripheral blood, appears usually in ring form. This plasmodium is the smallest of the three types. It is only 1 to 1.5μ in length when very young, and in later stages does not occupy more than one- to two-thirds of the erythrocyte. When from twelve to twenty-four hours old, the parasite appears as a pigmented, oval-shaped body. In stained preparations the parasitized erythrocyte may show granulations called *Maurer's dots*, which are well differentiated from Schüffner's dots by the fact that they are less numerous, more widely scattered, and coarser in appearance.

Asexual Reproduction.—Schizogony is completed in forty-eight hours, but it is less regular. Some parasites begin to sporulate after thirty-six hours; others sporulate after thirty-seven, thirty-eight, etc.,

up to forty-eight hours or more, and this fact accounts for the irregularity and protracted course of the fever; hence the name *pernicious malarial fever* which is also given to this type of infection.

Sporulation takes place in the internal organs—spleen, bone-marrow, etc.—and from eight to ten merozoites are formed (Plate VI). These are very small, measuring only about 0.7μ. The roset forms, except in very severe infections, are rarely found in the peripheral blood, but are readily seen in material obtained by splenic puncture at the onset of the chill.

Sexual Reproduction.—Under favorable temperature conditions (about 22° C.) sporogony is completed in about seven days in the body of the mosquito. The sexually differentiated forms (gametocytes) are found in the peripheral blood, and are easily recognized by their crescent shape (Plate VI).

Not infrequently, in stained preparations, the part of the erythrocyte covering the convex portion of these crescent-shaped gametocytes is seen to be relatively rich in hemoglobin as is evidenced by the fact that it is fairly well stained with eosin; on the other hand, in the concave portion of the parasite the corpuscle is pale and almost colorless, or visible merely as a delicate, semi-circular line stretching between the ends of the parasite. This probably proves that the gametocyte is not attached merely to the surface of the corpuscle, but that it lies within the erythrocyte, and that the reserve hemoglobin, with the stroma of the cell, has been gradually pushed aside and concentrated at the periphery of the cell during the growth of the parasite.

Manson describes three kinds of gametocytes as found in the peripheral blood: (1) The immature forms, which have a hyaline protoplasm; (2) the mature forms, which have a granulated protoplasm, especially marked in the macrogametocyte, and (3) the degenerated forms, whose protoplasm is vacuolated.

The *macrogametocyte* is recognized as a long, slender body; the cytoplasm is granular; the chromatin or nucleus is small and compact, and situated near the middle. It is characteristic of the macrogametocyte that the hemozoin is arranged in a circle around the nucleus.

The *microgametocyte* is shorter and broader in shape than the macrogametocyte; the cytoplasm is less granular or almost hyaline, and the nucleus is larger and richer in chromatin. The hemozoin is more widely scattered.

The formation of macrogametocytes and microgametocytes, conjugation, and the encystment of the oökinetes take place within twenty-four to forty-eight hours within the stomach of the mosquito.

On the second and third days the oöcyte appears as a clear, round body, the black hemozoin being aggregated into a clump and provided with a single nucleus. It grows rapidly, and on the fourth day the

cyst can easily be seen on the surface of the stomach under the low power of the microscope.

By the fifth or sixth day the *sporoblast* has increased considerably in size, and the sporozoites have begun to develop, and by the seventh day the cyst is full of sporozoites.

Between the eighth and tenth days the cyst ruptures, and the sporozoites can be found in the salivary glands and proboscis of the mosquito. These sporozoites become inoculated during the bite of the insect, and on reaching the circulation enter the erythrocytes, become trophozoites, and the cycle is repeated.

Mechanism of Infection.—The virus is transmitted to man by the bite of an infected mosquito. The infective stage in the life cycle of the parasite is represented by the sporozoite as found in the proboscis and salivary gland of the mosquito.

Pathogenesis.—Plasmodium falciparum is the cause of subtertian malarial fever in man. The disease is usually severe in nature, and in certain tropical countries not uncommonly proves fatal. The fever is not quotidian, but tertian in type, as it corresponds to the time of sporulation, which is completed in about forty-eight hours. As, however, sporulation may begin as early as within thirty-six hours in some parasites, and may be prolonged to forty-eight hours or possibly longer in others, it happens that the whole sporulation period consumes from twelve to twenty-four hours or longer, and as a consequence the febrile stage is prolonged at the expense of the quiescent period. This irregularity in time of the sporulation also accounts for the irregularity in the fever, and likewise explains the apparent quotidian type of the attack (Fig. 75).

In very severe infections, the fever may change, in the subsequent attacks, from the intermittent to the remittent or even the typhoid type, thus accounting for the pernicious character of the fever, which not uncommonly is accompanied by other grave symptoms, such as blocking of the cerebral capillaries by the parasites (Fig. 76).

Study of Gamete Forms.—For the observation of *gametes*, erroneously called *flagellated forms*, a case of chronic malarial fever that has lasted for three or more weeks and in the peripheral blood of which gametocytes are present in abundance, should be selected. A case of subtertian malarial infection is preferable, since in this type the crescent-shaped gametocytes are easily recognized; cases of tertian and also of quartan fever may, however, answer the purpose, provided the gametocyte is differentiated from the schizont by the characteristics previously described (pages 161 and 166).

A fresh cover-glass preparation is made, taking care not to use too much blood, so that the corpuscles can be easily separated. That part of the preparation between the center and the edge, where the

corpuscles appear fairly well scattered, should be selected for observation. A field should be chosen in which two or more mature microgametocytes are present, and which may be recognized by the scattered condition of the pigment, the granulation of the protoplasm, and the absence of vacuoles. The study should be made at room temperature (about 20° to 25° C.), and in about fifteen or twenty minutes the crescent-shaped microgametocyte will be seen to have become globular or round in shape. In time pseudopod-like projections begin to appear on the surface of the parasite; these gradually elongate



FIG. 76.—Section of the cerebellum from a case of malaria showing the malaria parasite *mp.*, lodged in the lumen of the blood capillaries.

and take on a spirochete-like shape. As they elongate they become actively motile, and finally become detached from the parent cell. These flagella-like bodies are the microgametes or spermatozoites. Three or four are produced from each microgametocyte.

If a permanent preparation is desired, remove the cover-glass, taking care to avoid any unnecessary disturbance of the blood; dry the preparation by swinging it in the air or by passing it rapidly through the flame; fix in equal parts of alcohol and ether or in methyl alcohol for about one minute, and stain by the Romanowsky (methyl-eosin) method or any of its modifications.

The Intracorpuscular Nature of the Malarial Parasite.—In the early days of our knowledge regarding the malarial parasite it was believed that the organism was merely attached to the surface of the erythrocyte. Some years later it was demonstrated that the parasite lived inside of the host cell, a view that is generally accepted today. The

DIFFERENTIAL CHARACTERS OF THE THREE SPECIES OF MALARIAL PARASITES

Species	P. malariæ or Quartan Parasite	P. vivax or Tertian Parasite	P. falciparum or Subtertian Parasite
Schisogony	Evolution complete in seventy-two hours.	Evolution complete in forty-eight hours.	Evolution complete in forty-eight hours more or less.
Merocites	From 6 to 12 in number and regularly arranged in a roset.	From 15 to 20 in number and regularly arranged.	From 8 to 15 in number and irregularly arranged.
Ring form	Intermediate in size, between *P. vivax* and *P. falciparum*; chromatin knob or nucleus not uncommonly inside of the ring. Parasitised erythrocytes usually contain only one ring.	Larger than the other two; nucleus in line with the ring. Usually only one ring is seen in the parasitised erythrocyte.	Smaller than the other two. Nucleus not uncommonly outside of the ring. Two or more ring forms may be seen in the same erythrocyte.
Young trophozoite	Intermediate in size between the other two. Movement very slow; pseudopodia inconspicuous; not uncommonly the parasite appears as an equatorial band across the erythrocyte.	Larger than the other two; movements very active; pseudopodia marked.	Smaller than the other two; actively motile; usually absent from the peripheral blood.
Hemosoin	Granules coarser, peripherally arranged, dark brown in color, and irregular in shape.	Granules finer; distributed through the parasite; yellowish brown in color; usually spiculated or rod shaped.	Granules very fine; scanty and brown in color; irregular in shape.
Schisont (matured trophozoite)	Intermediate in size; 6 to 7μ in diameter.	Very large—7 to 9μ in diameter.	The smallest of the three 4 to 6μ in diameter.
Changes in the parasitised erythrocyte	Almost normal in size or slightly retracted; when stained, is darker in color. Absence of granulations.	Larger in size; pale in color; presence of Schüffner's granules.	Smaller in size; stain dark; presence of Maurer's granules.
Gametocytes	Resembles the schisont, but larger in size, spheric in shape.	Resembles the schisont, but larger in size; spheric in shape.	Crescent in shape, rarely oval or spheric.
Clinical type of fever	Simple, double, or triple. Febrile stage lasts from four to eight hours.	Simple or double. Febrile stage lasts from four to eight hours.	Malignant, quotidian, remittent, or typhoid. Febrile stage usually protracted, lasting from twelve to twenty-four hours or longer.

facts in support of the intracorpuscular nature of the malarial parasite may be summarized as follows:

(1) The parasite and the parasitized erythrocyte appear to be focused on the same level under the microscope; (2) in other *Hemosporidia*, such as *Halteridium* (a parasite of birds), as the trophozoite increases in size it is seen to push the nucleus of the parasitized erythrocyte toward the periphery; this could not take place if the parasite were attached merely to the surface of the corpuscle; (3) sometimes the trophozoite of the malarial parasite may, it is true, actually appear on the surface of the erythrocyte, but this is undoubtedly a migratory phase of the parasite in the act of entering a new erythrocyte, when for some reason the host cell dies and the parasite is set free. Moreover, such forms are commonly seen in the subtertian parasite, but the gametocyte or crescent-shaped form of this type of malarial parasite shows a distinct accumulation of hemoglobin toward its convex surface, which indicates that the parasite, in its growth, pushes this substance and the stroma of the cell aside toward the periphery of the erythrocyte; (4) The malarial parasite, like other Sporozoa, Coccidium, most *Hemosporidia*, etc., is in all probability strictly intracellular in habit and can exist only inside of the host cell; finally, (5) Bass showed that prolonged contact with the serum of the blood is unfavorable or fatal to the malarial parasite.

THE DIAGNOSIS OF MALARIAL FEVER

Typical malarial infection, manifesting itself by sudden onset, the occurrence of chills, fever, and sweating, followed by a quiescent or an afebrile stage, and the reappearance, at regular intervals, of similar attacks, was first recognized by Hippocrates. Furthermore, the fact that whereas in some cases these attacks occurred every forty-eight hours, in others every seventy-two hours, and in still others, their course was protracted or irregular, although reported as occurring every forty-eight hours, led Hippocrates to differentiate the three types of malarial fever—namely, tertian, quartan, and subtertian.

This classification, being based chiefly upon the findings in acute cases, seen during the first weeks of the infection, when the periodic attacks have a tendency to be more regular, did not include a certain group of atypical chronic cases of malarial infection that may not present appreciable subjective or objective symptoms. The importation of quinin into Europe in the sixteenth century was an important factor in the recognition of these atypical cases and in the diagnosis of malarial infection in general. This drug, acting as a specific against the malarial parasite, served as a valuable means of differentiating malarial fever from certain allied diseases. Another difficulty, however, arose when it was found that quinin was useless in certain forms

of the disease. At the present time it is understood that although quinin is effective against the asexual forms of the malarial parasite (trophozoites), common to the early stage of the disease, it is ineffective against the sexual varieties (gametes) characteristic of chronic malaria.

The last link in the diagnostic chain in malarial fever was the discovery of the parasite in the circulating blood by Laveran in 1880. This discovery has not only greatly simplified the diagnosis of the disease, but has been of great importance in the prophylaxis of malarial infection. The finding of the parasite in the circulating blood is the only means of detecting certain chronic cases in which the sexual forms (gametes) which infect mosquitos are present. The technic is as follows:

1. Prepare a thin, dry blood preparation on a slide or cover-glass; dry and fix for one or two minutes in equal parts of alcohol and ether.

2. Stain with diluted borax-methylene-blue for two or three minutes.

3. Wash freely in running water for a few seconds. Dry, and examine under the oil-immersion lens of the microscope.

The malarial parasite appears stained a light blue, and the erythrocytes are pale green. Romanowsky, Wright, Giemsa, or any other polychromatic stain may be used, and although they give beautifully contrasting preparations, they possess no practical advantages over the method described (Plate VI).

Since in chronic cases of malaria the parasite is often present in such small numbers as to be undetectable in the small amount of blood usually examined, it is recommended that larger quantities of blood in concentrated preparations be used. Two methods, the one recently recommended by Bass and the other used by the author, may be employed for such purposes with good results.

The Author's Acetic Acid Concentration Method.—Collect about 0.1 c.c. of the patient's blood, drawn from the finger, in a narrow test-tube containing from 1 to 2 c.c. of a 1 per cent. acetic acid solution. Shake the mixture gently for from one to three minutes, or until complete hemolysis occurs; (2) centrifugalize for from ten to fifteen minutes, and pour out the liquid by carefully tilting the tube. The sediment remains at the bottom of the tube; (3) collect the sediment with a pipet; make slides or cover-glass preparations, and dry and fix in equal parts of alcohol and ether for from one to two minutes; (4) pour out the alcohol and ether, dry with filter paper, stain with diluted borax-methylene-blue for from two to three minutes, wash freely in running water, dry and examine under the oil-immersion lens. The malarial parasite is stained light blue, and is seen among the greenish stained detritus of erythrocytes. The leukocytes are stained a deep blue (Fig. 77).

This method is especially useful for detecting the gamete forms, and the author has used it with advantage in the diagnosis of malarial carriers in Brioni. With practice and by observing a careful technic, any of the forms of malarial parasite that may be present in the blood can be detected without difficulty.

Bass' Method.—(1) Collect 0.5 to 1 c.c. or more of the patient's blood, drawn from the finger, into a narrow test-tube containing an equal amount of an isotonic citrate solution; mix both liquids and centrifugalize for from ten to twenty minutes. The parasitized red blood-cells and the free malarial parasite (gametes of subtertian, etc.), being lighter than the remainder of the erythrocytes, will rise to the upper layer of cells; (2) carefully remove the supernatant liquid, and collect the upper layer, commonly known as the "cream of the blood,"



FIG. 77.—Semilunar bodies or gametes of malaria parasite (subtertian). Blood preparation made by the acetic acid concentration method.

in a pipet; (3) make dry spreads of the material on slides or coverglasses, stain by Wright's method, and examine under the microscope.

A more concentrated preparation may be obtained by further centrifugalization of the material in capillary tubes.

THE TREATMENT OF MALARIAL FEVER

The common knowledge that quinin is a specific against malaria has lead the medical profession in general, and the laity in particular, not only to the indiscriminate use of this drug, but also to regard it as the one and only measure in the treatment of the disease. Koch held the opinion that quinin was the only agent necessary for the treatment, prophylaxis, and the eradication of malaria from a community. In 1899 he advocated the use of this drug to the exclusion of all other prophylactic measures for the sanitation of Brioni. After the work of the first year, it was found, owing to the recent discov-

eries of Schaudinn, Ross, and Grassi, that, in addition to quinin other prophylactic regulations must be carried out in order to accomplish the desired end.

That quinin is a specific against malaria there can be no doubt, but, as in the case of other specifics, it is the proper use of the drug and not its abuse that effects a cure. For the correct and rational use of the drug the following points should be taken into consideration: (1) The preparation used; (2) the mode of administration; (3) the dosage; (4) the time of administration; (5) the duration of treatment.

1. **The Preparation Used.**—Generally speaking, quinin sulphate should be preferred for internal administration, and quinin bimuriaticum for hypodermic injections.

2. **The Mode of Administration.**—As a routine procedure, quinin should be given by mouth, the drug having previously been dissolved in diluted hydrochloric acid. The administration of quinin in the forms of pills, capsules, cachets, etc., is not to be recommended, since not uncommonly they pass through the digestive tract undissolved; moreover, since this alkaloid is absorbed chiefly in the stomach, a capsule or pill may readily pass undissolved to the small intestine. For the same reason, in the acute stage of malarial fever and in the subsequent treatment, or when given as a prophylaxis, as outlined below, quinin should preferably be given on an empty stomach—if possible, about four or five hours after meals, in the evening before retiring, or in the morning before breakfast, the drug being thus more rapidly absorbed.

When indicated, hypodermic injections are to be preferred to intravenous injections, the latter being used only in case of emergency in very severe and grave cases. Hypodermic injection is especially useful in those cases in which administration by the mouth gives rise to nausea and vomiting or to diarrhea, or when these complications accompany the disease, as in "bilious remittent fever," etc.

3. **The Dosage.**—For an adult, not less than 15 grains (one gram) should be given in a single dose. Twenty or even 30 grains may be given in severe or grave cases of subtertian fever, when this dose is well borne by the patient. For a child from one to ten or fifteen years old, one to ten or fifteen grains respectively are given—that is, one grain for each year. The use of small doses, such as two grains repeated at intervals, commonly prescribed for adults, is contraindicated, for the reasons given below.

4. **The Time of Administration.**—One of the most important points to be considered for the successful treatment of malaria is the time at which quinin should be given. From our knowledge concerning the asexual cycle of the malarial parasite in the body, and knowing, as we do, that the sporulation stage corresponds to the chill, and the

entrance of the merozoites in the erythrocytes to the febrile stage; because of the fact that not all the parasites sporulate at the same time, and the period may last for from four to eight hours in tertian and quartan and a longer time in subtertian; that the fall in the temperature or crisis corresponds to the early growth of the trophozoite stage; that the afebrile period, which lasts from forty to forty-four hours in tertian, from sixty-four to sixty-eight hours in quartan, and from twelve hours or less to twenty-four hours or longer in subtertian, and during this time the trophozoite develops into a schizont, when sporulation again occurs and the cycle is repeated—all these facts clearly show that the clinical manifestations of a malarial attack are controlled or correspond to the different phases of the asexual cycle of the malarial parasite in the body. For practical purposes, therefore, the cycle of the attack may be divided into four stages, namely: (1) Chill—sporulation; (2) fever—entrance of merozoites into the erythrocytes; (3) crisis—beginning growth of the trophozoite; (4) afebrile period—further growth of the trophozoite up to the schizont stage.

With these points in mind, it is reasonable to assume that *the most favorable time for the administration of quinin is during the third stage, or the crisis, at the time when the temperature begins to fall.* Among other reasons that point to administration at this stage two which are most important may be given: (1) At this stage the parasite is very young, and consequently is easily destroyed by the drug; (2) at this stage, when the parasite begins its growth and its metabolic activity is at its highest, it is natural to assume that it is more apt to take a larger amount of quinin than when it grows older and becomes quiescent. This biologic fact is manifested in all forms of life, and explains, for instance, why a child consumes proportionally five times as much food as an adult, and why it is likewise more susceptible to the action of drugs, of which narcotics may be cited as an example.

As the parasite grows older, therefore, it becomes less susceptible to the action of quinin until it reaches the schizont stage, when, like the gametes, it may be said to be refractory to the drug.

The sporulation stage may likewise be said to be refractory to the drug, because as may readily be understood, the merozoites represent merely a quiescent stage between the schizont and the young trophozoite (plasmodium) stages. During this period the merozoite enters the erythrocytes and remains quiescent for some time before it becomes adapted to the new environment and begins to develop.

The fact that the malarial parasite remains dormant in the merozoite or ring stage for some time (from six to twenty-four hours or longer) after it enters the erythrocyte during the chill is explainable, perhaps by a peculiarity in the life history of the parasite. It should not, however, be forgotten that the high temperature of the body at

this stage (103° to 104° F.—39° to 40° C. or over) is unfavorable for its metabolic activity and growth. If this view is correct—and the writer believes it to be at least a contributing factor, basing his conclusions upon a single observation—it seems that the artificial lowering of the temperature of the body shortly after the chill, as by a cold bath or suitable medication, would cause an earlier growth of the schizont, and hence the administration of quinin at this point would tend to shorten the attack. The point is worth while considering, especially in the management of those pernicious types of subtertian malarial infection in which the febrile period is prolonged.

The foregoing facts regarding the life cycle of malarial parasites, can clearly show that the essential point in the successful treatment of malarial infection is not the indiscriminate use of quinin, but the rational use of the drug—that is, administration at the proper time,

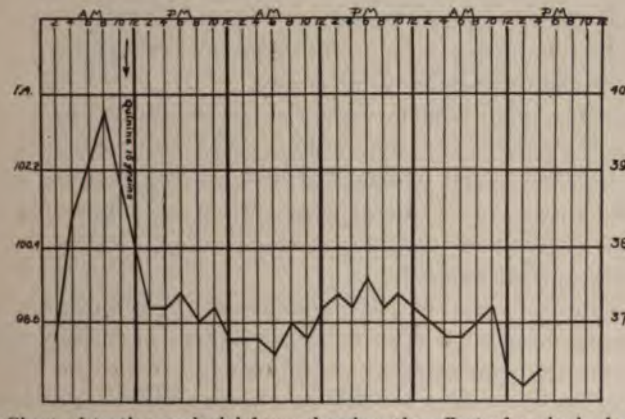


FIG. 78.—Chart of tertian malarial fever showing the effect of a single dose of quinin (1 gm.) given at the proper time in preventing subsequent recurrence of the attack.

when the parasite is beginning to grow. Of course it is difficult, especially in field work or in atypical cases of malarial fever to follow this indication, but under these unfavorable circumstances a single microscopic examination of the blood will suffice in most cases to determine the kind and approximate age of the parasite, and to permit a prediction to be made with sufficient accuracy as to the time of the subsequent attack, and accordingly to instruct the patient as to the time when quinin should be taken.

It is advisable too, when possible, especially in hospital work, to control the clinical manifestations of an attack of malaria by making a microscopic examination of the blood at stated intervals.

The line of treatment as here outlined has been followed by the author in all the cases of malarial infection in Brioni and elsewhere in the tropics that have come under his care, with most successful results,

and he has often seen a single dose of quinin, when given at the proper time, completely avert subsequent attacks (Fig. 78).

5. **The Duration of Treatment.**—The successful treatment of malarial infection depends upon the continued administration of quinin for a certain length of time. A single dose of quinin may suffice to guard the patient against a subsequent attack, but only temporarily, as usually the fever reappears after weeks or months. To avert these recurring attacks the following rule should be followed: Give 15 grains of quinin when the fever begins to decline, and repeat the dose for three successive days at the same hour. No quinin should be given during the following four days, after which the treatment is again repeated—that is, 15 grains are given for the following three successive days, after which no quinin is given for the following four days, and so on. The treatment, therefore, consists in giving 15 grains of quinin for three successive days every week, and continuing this for not less than two, and preferably three, months, after which the prophylactic treatment of 10 grains of quinin once every week should be given for the remainder of the season.

The treatment of chronic malarial fever—those cases that show gametes in their blood, or those of long standing in which the parasite may not be found, and which clinically present organic lesions and constitutional and other disturbances, such as enlarged spleen and liver, gastro-intestinal derangements, marked degrees of anemia, etc.—is very unsatisfactory.

Tonics in the form of iron and arsenic are recommended. Of chief importance in such cases is the avoidance of subsequent attacks or of reinfection, which aggravate the condition, by the prophylactic administration of quinin, and, when possible, the reinfections should be prevented by the removal of the patient to a non-malarial district, preferably to a high altitude or to a northern climate.

THE PROPHYLAXIS OF MALARIAL FEVER

Summing up our present knowledge concerning malarial fever and the life history of the plasmodium we arrive at the following conclusions, namely: That while quinin is a valuable specific against the asexual forms of the parasite, it has no effect on the sexual forms or gametes; that these sexual forms, when imbibed by the mosquitos while biting, undergo evolution in the body of the insect, and the parasite is thus transmitted to man through the bite of the infected mosquito. The prophylactic measures against malaria may be summarized as follows: (1) Routine blood examination; (2) treatment by quinin; (3) proper care of the malarial carrier; (4) destruction of mosquitos; (5) quinin prophylaxis.

1. **Routine Blood Examination.**—The attention of the parasitologist and hygienist should be directed first to the examination of the blood of all persons in the community if possible, as a routine procedure. The importance of this preliminary precaution can readily be understood, since it is the only means of obtaining the first and most thorough insight into the kind and degree of infection present, upon which will be formulated the future plans for sanitation of the place in question.

2. **Treatment by Quinin.**—All persons in whose blood malarial parasites are found, whether or not they present symptoms of the disease, should be treated with quinin in the manner previously outlined.

3. **Proper Care of the Malaria Carrier.**—In order to prevent the spread of the infection all malarial carriers—those that show the presence of the gamete forms of the parasite in their blood—should be isolated or removed to non-infected places that are free from mosquitos, if possible. Not uncommonly this important precaution is difficult or impossible to carry out, but under these circumstances the same results may easily be accomplished by instructing the patients to sleep under mosquito netting in order to prevent mosquito bites.

4. **Destruction of Mosquitos.**—Mosquitos are easily and most effectually destroyed in the larval stage by the application of about 1 c.c. of petroleum to the square meter surface of water. The oil should be applied to all ponds, slowly flowing creeks, stagnant pools, etc., regularly at least once a week.

5. **Quinin Prophylaxis.**—This simple and efficient means for the prevention of malarial fever, as advocated by Koch, consists in the taking of from 10 to 15 grains of quinin, previously dissolved in water acidulated with hydrochloric acid, once or twice a week during the summer months.

This brief and simple outline concerning the diagnosis, treatment, and prophylaxis of malarial fever, is the one which the author followed in his work of improving the sanitation of Brioni during the years 1901 and 1902, with the result that, after three summers had passed, the island was declared completely free from the disease. It is, moreover, the best evidence of the marvelous progress which tropical medicine and parasitology, thanks to the discoveries of Laveran, Manson, Ross, Grassi, Koch, Schaudinn, and many other workers in the field, have made in recent years. The sanitation of Brioni stands preëminently as an example of what may be accomplished by the careful and systematic appliance of modern prophylactic regulations, by means of which malaria was for the first time successfully eradicated from a community.

The application of this prophylactic regulation rendered possible the sanitation of the Canal Zone in Panama, and has greatly improved the sanitary condition of other tropical countries here in America as well as abroad.

It is to be hoped that the various governments and individual philanthropists, moved by the highest of humanitarian principles —the health and happiness of mankind—will in the near future direct their energies toward helping those unfortunate countries of tropical America that still labor under the burden and oppression of this disease—a disease that has for centuries hindered the development of the natural resources of these regions, to say nothing of the physical and mental well-being of their inhabitants.

Stimulated by the discoveries of Pasteur, modern medicine has accomplished much in the control and practical eradication of a number of bacterial diseases, such as diphtheria, typhoid fever, tetanus, and others. This fact lends a hope that the day is not far distant when the doctrine established by the French genius will be an accomplished fact: "C'est dans le pouvoir de l'homme de fair disparaître tous les maladies infectieuses de la terre," and, we may add, the eradication of tropical and parasitic diseases from tropical countries.

HEMOSPORIDIA OF THE LOWER ANIMALS

GENUS PLASMODIUM (Marchiafava and Celli, 1885)

1. **P. kochi** (Laveran, 1899).—A parasite found in chimpanzees and monkeys in Africa and Ceylon. Inoculable from one animal to another. Sporogony unknown, despite numerous experiments made with *Culex* and *Anopheles*. It causes illness and death in monkeys.

2. **P. inui** (Halberstaedter and Prowazek, 1907).—Found in *Macacus cynomolgus* and *M. nemestrinus*. Merozoites number 12 to 16. Schüffner's dots absent.

3. **P. cynomolgi** (Mayer, 1907).—This is probably identical with *P. inui*, except that Schüffner's dots are present.

4. **P. pitheci** (Halberstaedter and Prowazek, 1907).—Found in the ourang-utang and chimpanzee; resembles *P. vivax*, but is not inoculable to man. Schüffner's dots are present.

5. **P. brasilianum** (Gouder and Berenberg-Gossler, 1908).—Found in monkeys in South America. Morphologically it resembles *P. malariæ* in man.

6. **P. canis** (Castellani and Chalmers, 1908).—Found in the erythrocyte of the dog in India; resembles *P. vivax*.

7 **P. danilewskyi** (Grassi and Feletti, 1890).—Found in the erythrocyte of birds in Italy and in sparrows in India. It is common in

Africa. This is the parasite in which Ross first traced the development of the plasmodium in the mosquito.

Several other species of plasmodium have been found in birds and reptiles.

GENUS HEMOPROTEUS (Kruse, 1890)

The Hemoprotei are Sporozoa found in the blood of birds, and somewhat resembling the malarial parasite. According to Schaudinn, the Hemoprotei are differentiated from the Plasmodium by the fact that they have a more complex evolution. Schaudinn believed that these parasites on reaching the stomach of the mosquito, were metamorphosed into trypanosomes, a view that is not generally accepted. Another point in the differentiation is the fact that the Hemoproteus (Halteridium) does not produce sporozoites, but gives rise to very small, trypaniform-like bodies (probably invisible) which transmit the virus to susceptible animals (Schaudinn). The following are some of the species of this genus:

1. **Hemoproteus noctuæ** (Celli and Sanfelice, 1898).—Commonly called Halteridium. This parasite is found in the erythrocyte of the little owl (*Glaucidium noctuæ*). The asexual cycle takes place in the blood of the owl, and the sexual evolution (sporogony) in *Culex pipiens*.

Sporogony.—Both macrogametocytes and microgametocytes appear inside of the erythrocyte as a typical Halteridium, with pigmented protoplasm, and provided with a single large nucleus containing trophic and kinetic elements.

The Microgamete.—The microgametocyte leaves the erythrocyte in the stomach of the mosquito, throws out active flagella, and finally becomes free in the form of a typical trypanosome provided with an undulating membrane and a flagellum. The trophonucleus is large and elongated, and occupies the main part of the body, and the kinetonucleus is situated toward the non-flagellated end of the parasite.

The Macrogamete.—The macrogametocyte, which also leaves the erythrocyte, is a round body; it undergoes reduction and maturation.

Zygosis.—This consists in the penetration of the trophonucleus and kinetonucleus of the microgamete into the macrogamete. The male and female trophonuclei now fuse and form the fusion spindle, at either end of which the kinetonuclei take up their position.

Oökinete.—The zygote becomes motile, assumes a vermiform shape, pointed at one end, and develops into an oökinete. According to Schaudinn, there are three kinds of oökinetes: (1) Indifferent oökinete; (2) male oökinete; (3) female oökinete.

1. *Indifferent Oökinete.*—The indifferent oökinete is recognized by its clear cytoplasm and by the presence of one or two large vacuoles. Hemozoin is scanty. By a complicated process of nuclear division it develops into an indifferent trypanosome, which now multiplies

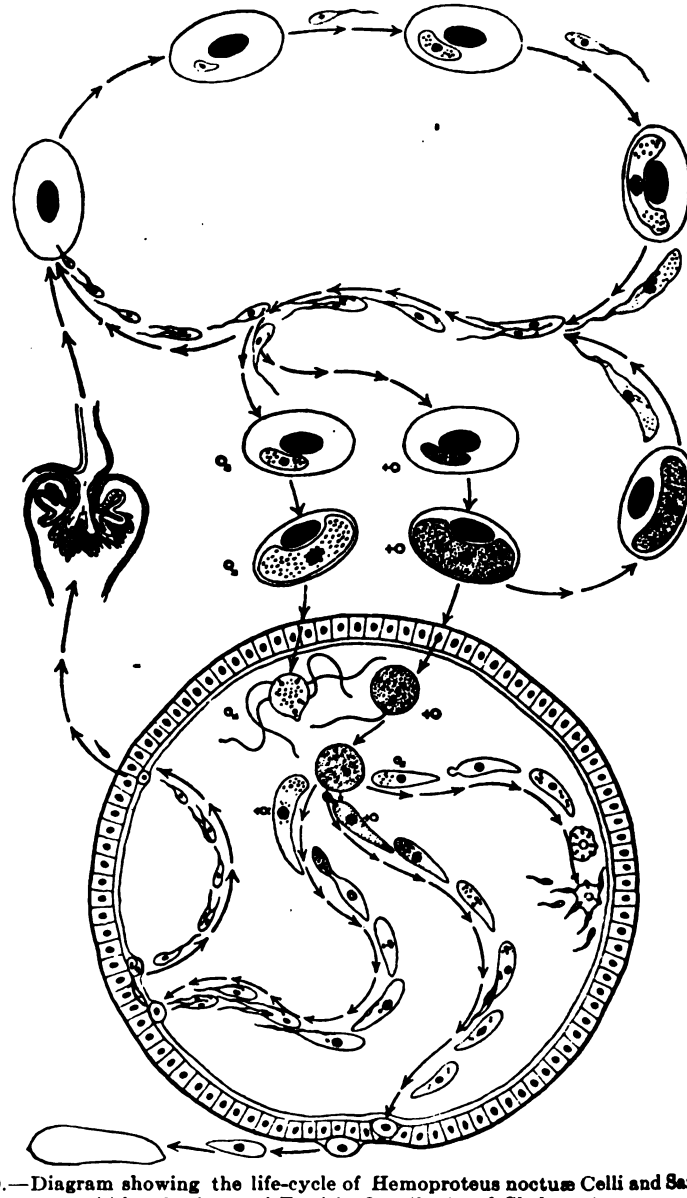


FIG. 79.—Diagram showing the life-cycle of Hemoproteus noctuæ Celli and Sanfe
(After Sambon and Terzi in Castellani and Chalmers.)

by binary fission. After a time it assumes a gregarine form phase, and attaches itself to the epithelial cell of the stomach of the mosquito by the flagellum. In this position it may further multiply or penetrate the epithelial layer, lose the flagellum, and become encysted. After a period of rest it becomes active again and either enters the blood of the little owl and becomes differentiated into male and female forms, or eventually dies.

2. *The Male Oökinete.*—The male oökinete is recognized by the fact that it is smaller than the other two forms, and by having a large nucleus, rich in chromatin. By a process of nuclear division it gives rise to male and female elements. The female or larger portion disappears, and the male portion gives rise to tiny male trypanosomes, after which it also dies and disappears.

3. *The Female Oökinete.*—The female oökinete is recognized by its dense and granular cytoplasm and relatively small nucleus. Like the male oökinete, by a process of nuclear division it gives rise to female and male forms, but in this the small male forms degenerate, whereas the female gives rise to a female trypanosome as in the indifferent form of oökinete. These female trypanosomes move slowly and do not divide, but take on a gregarineform shape. They remain quiescent for a time between the epithelial cells, or pass to the ovaries and eggs of the mosquito and lie dormant during the winter.

The female oökinete may also undergo parthenogenesis and give rise to indifferent male or female trypanosomes.

Schizogony.—Asexual reproduction takes place in the blood of the little owl. All three forms, male, female, and indifferent trypanosomes, found in the body of the mosquito, as previously described, may enter the owl through the bite of the insect, but the indifferent types predominate. On passing into the circulation these indifferent trypanosomes divide and enter the erythrocytes. The parasite now loses its flagellum and develops into a young halteridium. After twenty-four hours a flagellated type is reformed, which then leaves the erythrocyte, usually at night as a typical *Trypanosoma noctuæ*. After a time it reënters another erythrocyte, and continues to grow until the next night, when it again leaves the erythrocyte, the process being repeated about six times before the trypanosome becomes fully grown. It now undergoes division into small forms of trypanosomes outside the erythrocyte, thus completing the cycle of schizogony. These small forms now enter a new cell as before, and the cycle is repeated.

In *Hemoproteus noctuæ*, therefore, the merozoites are represented by the small extracellular trypanosome forms; the trophozoite, by the grown intracellular halteridium; and the schizont by the fully grown and large extracellular trypanosome. The sexual forms, as in the malarial parasite, are developed from these merozoites (indiffer-

ent small trypanosomes), which, on entering the erythrocyte, grow and become differentiated into macrogametocytes and microgametocytes, etc., thus completing the cycle of sporogony in a manner similar to the malarial parasite, except that in hemoproteus indifferent trypanosomes are formed in the body of the mosquito instead of sporozoites.

This life cycle of *H. noctuæ*, as described by Schaudinn, points to the close relation which perhaps exists between the *Hemosporidia* and the flagellates. "Schaudinn's view has not been proven *in toto*, especially as to the point of the exchange of trypanosoma into halteridium and *vice versa*." It is, however, a known autogenetic fact that, with the exception perhaps of very primitive forms of life, such as certain bacteria and rhizopods, or in a few higher parasitic forms, such as ascaris, all living beings exhibit a flagellated phase at some time in their life history. This takes either the form of the spermatozoite or spermatozoön, which in many ways, morphologically at least,



FIG. 80.—Hemoproteus noctuæ Celli and Sanfelice. (*After Schaudinn in Castellani and Chalmers.*)

bears a great resemblance to a trypanosome, a fact that has lead biologists to regard the flagellates as the ancestors of all higher forms of parasitic life. If Schaudinn's work on *Hemoproteus noctuæ* is found to be correct, it will not only prove the close relation that exists between the *Trypanosomidæ* and the *Hemosporidiæ*, but will tend to show that the latter have probably been derived from the former, and that the malarial parasite represents a higher, more specialized parasitic type of trypanosoma.

2. **H. passeris** (Celli and Sanfelice, 1890) is the Halteridium found in the blood of the sparrow.

3. **H. columbæ** (Celli and Sanfelice, 1891) is the Halteridium found in pigeons (*Columba livia*).

4. **H. danilewskyi** (Kruse, 1890) is found in the blood of the crow (*Corvus cornix*).

A large number of other species of *Hemoproteus* have been described in birds and reptiles.

GENUS LANKESTERELLA (Labbe)

This parasite is found in the erythrocyte of the frog. The best known form is *L. ranarum*.

GENUS LEUKOCYTOZOÖN (Danilewski, 1889)

The Leukocytozoa are blood parasites found in the erythrocytes, hematoblasts, or leukocytes of birds. They are characterized by the absence of hemozoin. In the peripheral blood only the gametocytes are found, and schizogony probably takes place in the internal organs. The following are some of the best known species.

1. **L. danilewskyi** (Zieman, 1898).—This parasite, also called *L. ziemanni*, is found in the hematoblasts and leukocytes of the little owl (*Glaucidium noctuæ*) and the wood-owl (*Syrnium aluco*). *Culex pipens* acts as the intermediate host of the parasite.

2. **L. smithi** (Laveran and Lucet, 1905) is found in the domestic turkey, *Meleagris gallopavo domestica*.

3. **L. macleani** (Sambon, 1908) is found in the common pheasant (*Phasianus colchicus*).

4. **L. sakharoffi** (Sambon, 1908) is found in the crow (*Corvus cornix*).

GENUS BABESIA (Starcobici, 1893)

The *Babesia*, commonly called *Piroplasm*, are parasites of the blood. They are found in the erythrocytes in the form of pear-shaped bodies. Schizogony takes place in the erythrocytes by fission or gemmation, with the formation of rounded or pyriform merozoites. Sporogony is not well known, but takes place in ticks, in which the virus is transmitted by infecting the egg of the adult female tick to the next generation. Some of the best known species are the following:

1. **Babesia canis** (Piana and Galli-Valerio, 1895).—In fresh blood preparations this parasite appears as an irregular, ameboid or pear-shaped body, brown or dark in color, having a central refracting portion. One, two, or more parasites may be found in the same erythrocyte, and the organism may also be seen free in the plasma. The parasitized erythrocyte appears swollen and pale. In preparations stained by the Romanowsky method or one of its modifications the parasite is seen to consist of a blue cytoplasm, a red-stained nucleus, and a vacuole at the center.

Schizogony.—The common process of asexual reproduction consists in the entrance of the free pyriform parasite—*pyriform or merozoite stage*—in a normal erythrocyte, in which the young trophozoite takes the ring form—*ring stage*. It now grows, becomes ameboid

and vacoluated—*ameboid stage*—and after some time the nucleus divides and the parasite enters upon a period of rest—*quiescent stage*. One of the chromatin masses now divides, and this is followed by segmentation of the cytoplasm and the vacuole, and the so-called *trefoil stage* is reached. The parasite now presents a clover-leaf appearance, and consists of two small chromatin masses connected by chromatin strands, two vacuoles, with a main chromatin mass at the center.

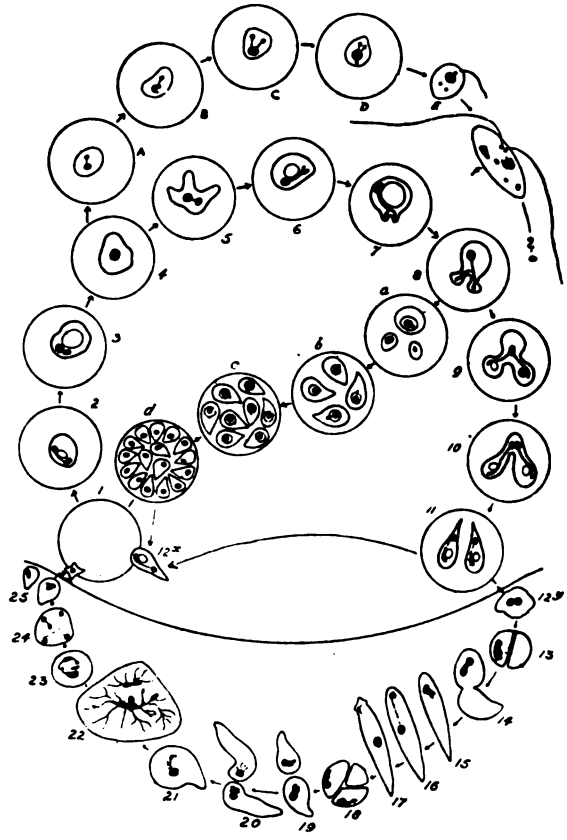


FIG. 81.—Diagram of the life-cycles of Babesia canis. (*After Nuttall and Graham-Smith, Christophers, and Breinl and Kinghorn.*) 1–12*x*, Reproduction by simple division; *a*–*a*, reproduction by multiple division; A–F, development of a flagellate form; 12*y*–25, sporogony in the tick. (*In Castellani and Chalmers.*)

The chromatin strands now disappear; the main chromatin mass divides, followed by segmentation of the cytoplasm and the formation of two pyriform parasites lying side by side within the erythrocyte. This arrangement is considered typical of *Babesia*. Each parasite, therefore, consists of a cytoplasmic mass, pyriform in shape, containing a vacuole, a principal chromatic nucleus, situated toward the pointed

end, with a loose chromatin stand alongside the vacuole, toward the blunt extremity. The corpuscles now rupture, and the two parasites, set free, enter other erythrocytes and the cycle is repeated.

Instead of two, four pyriform parasites may be found in the same erythrocyte. This is due probably to the primary invasion of the corpuscle by two pyriform bodies, or to the division of the uninuclear ameboid stage into two organisms, each of which proceeds to develop regularly

Reproduction by multiple division may take place and give rise to several small pyriform bodies. Reproduction by gemmation has been described by Breinl, Hindle, and Kinoshita.

Flagellated forms, the significance of which has not been determined have been described by several authors.

Development in the Tick.—When the pear-shaped bodies just described are ingested by the nymph or adult tick, the parasite undergoes development in the intestine of the tick, and becomes a round or oval body 4 to 5 μ in diameter; it gradually elongates and becomes an *oökinete*. In the adult tick the oökinete passes into the ova, whereas in the nymph it simply passes into the embryonic tissue. In either case the oökinete develops into a sporoblast, and finally gives rise to sporozoites which invade the salivary glands and other parts of the body, as well as the ovaries and eggs, thus carrying the virus to the second generation.

Mechanism of Transmission.—The parent tick, becoming engorged with infected blood, falls to the ground and lays her eggs, which hatch six-legged larvæ. These larvæ feed on the dog for two days, sucking its blood, and eventually drop off; in due time they molt and become eight-legged nymphs. These again feed on the dog, drop off once more, undergo metamorphosis, molt, and become sexually mature. According to Landsburg and Nuttall, the virus is not transmitted by the larva nor by the eight-legged nymph, but only by the adult tick.

Pathogenesis.—Babesia canis is the cause of a specific infection in the dog characterized by fever, weakness, anemia, jaundice, and hemoglobinuria. In young dogs it usually terminates in death in from three to six days. Often, especially in adult dogs, the disease runs a benign course and ends in recovery.

2. **Babesia bigemina** (Smith and Kilbourne, 1893).—This parasite is found in the blood of cattle, and is the cause of Texas cattle fever. The morphology and life history of the parasite are similar to those of *B. canis*. The parasite has been cultivated artificially. It is transmitted by several kinds of ticks (*Margaropus australis*, *M. decoloratus*, etc.) infected by the presence of the parasites in the eggs of the mother.

3. **B. ovis** (Babes, 1880).—A parasite found in the blood of sheep. It causes anemia, hemoglobinuria, and hematuria in the infected animal.

4. **B. bovis** (Babes, 1888).—This parasite is found in the blood of cattle, and is the cause of red-water or hemoglobinuric fever in European cattle.

5. **B. parva** (Theiler).—This parasite is the cause of East Coast fever in cattle in Rhodesia. It is also found in India and Japan. It appears as a small, bacillus-like organism called *Theileria* by some writers, or as a ring or pyriform body within the erythrocyte.

6. **B. equi** (Laveran, 1899).—This parasite is found in horses.

7. **B. hominis(?)** (Manson, 1903).—In 1902 Wilson and Chowning described small, ovoid, and ameboid or pyriform intracorpuscular bodies in the blood of man in cases of spotted fever of the Rocky Mountains. They suggested that the disease was transmitted by the tick. Ricketts and King have been able to transmit the disease to monkeys and guinea-pigs by means of the adult tick (*Dermacentor occidentalis*), and Marx and McCalla and Brereton have transmitted the disease twice from man to man by the tick.

8. **Bartonella bacilliformis.**—This is the parasite of Oroya fever of Peru discovered by Burton, of Lima, in 1905 and studied by the Harvard expedition in 1913 and 1914.. Strong and his associates describe the parasite as occurring in the erythrocytes and endothelial cells as minute coccoid bodies measuring 0.5 to 1.0μ in diameter or as short bacillary forms measuring 1.5 to 2.5μ in length. The microörganism is motile and in severe infection several parasites may be found in the same corpuscle.

Dr. Strong and his colleagues believe the parasite to be a protozoa, probably a sporozoa related to the *babesia* (piroplasmata) or Texas fever parasite of cattle, but its classification cannot yet be determined.

Multiplication takes place in the endothelial cells of the lymph glands and spleen, but the method of transmission is still in doubt. It has been suggested that like Texas fever, Oroya fever may be transmitted by a tick or some other arthropodes.

Our present knowledge concerning Rocky Mountain fever is that it is transmitted by the tick (*D. occidentalis*). Nothing definite is known regarding the nature of the parasite. Ricketts has recently reported the finding of bacillus-like bodies.

GENUS HEMOGREGARINA (Danilewski, 1885)

The hemogregarines (Fig. 82) are blood parasites. They are usually found either in the erythrocytes or in the leukocytes, but they may also appear free in the plasma or in the cells of the liver, spleen, lung, etc. Morphologically they are elongate or vermiform, not uncommonly

striated, and consist of a mononucleated mass of granular cytoplasm provided with an envelop made up of an outer and an inner layer. It is *characteristic of the hemogregarine, the absence of pigment, hemozoin, in the protoplasm, a feature which differentiates them from other hemosporidia such as the malarial parasite.*

Reproduction takes place asexually inside of the parasitized cell, with the production of several merozoites, which upon being set free, enter a new cell and repeat the asexual cycle. Or the merozoite may enter a leukocyte, become encysted, develop into a gametocyte and undergo sexual reproduction—*sporogony*—as in Coccidia. Coccidia, however, require only one host, whereas sporogony in hemogregarines begins in the vertebrate—the primary host—and is completed in an intermediate host—an insect, tick, mite, etc. This fact, together with the absence of a trypanosome stage in *Hemogregarina muris* (Miller), and the absence of *hemozoin* in the parasite, indicates that the hemogregarines are related to the gregarines and Coccidia.



FIG. 82.—Diagram of hemogregarine.

Hemogregarines are common parasites of the lower vertebrates, several species having been described. They are found so abundantly in reptiles that these animals are especially recommended for their study. Some of the best known species are the following:

1. **Hemogregarina canis** (James, 1905).—This organism is a parasite of the dog. As seen in the leukocyte it appears as an oval, uninucleated, and unpigmented body, that is difficult to stain. It is inclosed in an envelop made up of two layers—one external, formed by the host cell, and the other internal, belonging to the parasite.

Schizogony.—This takes place in the bone-marrow, and consists in the reproduction of about 30 merozoites. On being set free, these merozoites enter new cells, and the cycle is repeated; others become encysted in the leukcocytes, and develop into gametocytes(?).

Sporogony.—According to Christophers, sporogony takes place in the tick—*Rhipicephalus sanguineus.* The encapsulated forms, found in the leukocyte, as previously described, on being taken into the stomach of the tick are set free, become elongated, and finally enter the epithelial cells of the gut, where they multiply, giving rise to from four to eight undifferentiated secondary vermicular bodies. Two of these bodies now conjugate and deevlop into an *oöcyte.* The oöcyte gives rise to numerous vermicular bodies (sporocysts or sporoblasts), which are finally set free in the lumen of the gut. The mode of entrance of these bodies into the dog has not been determined.

2. **H. bovis** (Marfoglia and Carpano, 1906).—This parasite is found in the blood of oxen (*Bos taurus*) in Abyssinia.

3. **H. muris** (Miller, 1908).—This is a cosmopolitan parasite, found in the leukocytes of the rat, *Mus norvegicus*, and in the white rat.

4. **H. felis** (Adie, 1906).—This parasite is found in the cat. A great number of other species have been described, some being found in birds, fish, and especially in reptiles.



FIG. 83.—Sarcocystis rileyi in pectoral muscle of wild duck.

III. THE SARCOSPORIDIA

The *Sarcosporidia* are found in the muscles of warm-blooded animals, birds, mammals, etc., but seldom in man. Reproduction takes place by sporulation, which begins early and continues during the entire life of the parasite, which may reach a relatively large size, so as to be easily seen with the naked eye.

When fully grown, the parasite, commonly known as *Sarcocyst*, appears as a cyst or tube, according to



FIG. 84.—Sarcocystis rileyi in pectoral muscle of duck. Low power photomicrograph showing longitudinal section of sporocyst at *a*, and transverse one at *b*. A constriction, probably at base of a bud, is seen at *c*.

the species. It is covered by a cyst-wall, which consists of an external layer, the cuticle, made of the condensed tissue of the host, and

an internal layer formed by the parasite. This internal layer is continued into the cyst in the form of delicate trabeculæ or fibrillæ which divide the cyst into several chambers containing parasites in different stages of development—*e.g.*, *sporoblasts*, *spores*, etc.

Under the lower power of the microscope the inside of the cyst is seen on section to be divided into two main zones—an outer *cortex*, or *proliferative zone*, containing the parasite in different stages of development, and a *central core* which contains the spores—*merozoites*—in varying degrees of degeneration and disintegration.

The spores are usually naked. They are from 1 to 12μ in length, according to the species, and are either globular or crescent shaped.

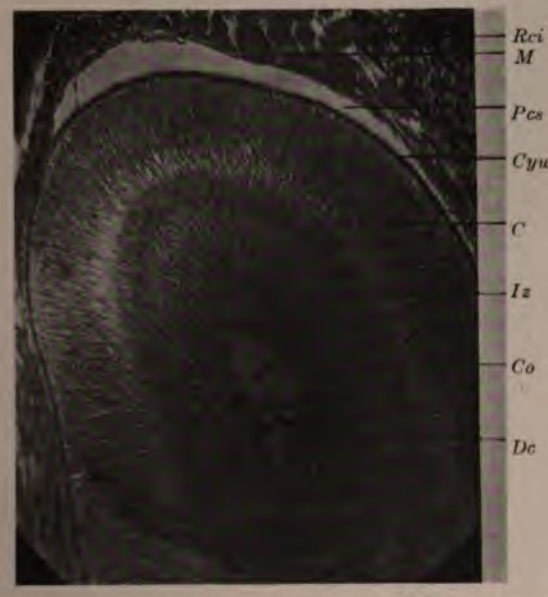


Fig. 85.—Sarcocystis rileyi in pectoral muscle of duck. Photomicrograph of part of sporocyst. *Rci.*, round cell infiltrate; *M.*, muscle; *Pcs.*, pericystic space; *Cyw.*, cyst wall; *C.*, cortex; *Iz.*, intermediate zone; *Co.*, core; *Dc.*, degenerated centre.

Structurally they consist of a granular cytoplasm containing a single nucleus and one, two, or more vacuoles.

These spores are regarded by many observers as the means by which the parasite infects the surrounding tissue, and they are also believed to represent the infective stage of the parasite. In what manner they are transmitted to another host is not known.

Some authors describe two kinds of spores, namely, gymnospores and clamidospores; both kinds are, however, apt to occur, depending on the species, and it is also probable that they merely represent developmental stages—the gymnospores (naked spores) representing

a younger stage (merozoites), and the chlamydospores, older forms, or *spores proper* (Minchin).

Life History.—The life history of *Sarcosporidia* is not well understood. It is believed that the spore represents the resting stage of the parasite, but the manner in which this spore gives rise to a new growth is not clear. It is probable that, as in other Sporozoa, the spore, under certain conditions, undergoes development, becomes a trophozoite, and appears as an irregular or round mass of cytoplasm containing a single nucleus. As it grows the trophozoite becomes a sporoblast or *pansporoblast* (a multinucleated schizont), which by further division and differentiation gives rise to numerous spores.



FIG. 86.—Sarcocystis rileyi. Drawing of part of sporocyst and adjacent host tissue showing developmental stages of contained spores, *M*, muscle; *Rci.*, round cell infiltrate; *Pcs.*, pericystic space; *Cpt.*, condensed pericystic tissue; *Cyw.*, cyst wall; *Cs.*, layer of condensed stroma; *Sf.*, zone of spore formation; *Ms.*, zone of mature spores; *Deg.*, zone of degeneration; *Dc.*, degenerated centre.

It is characteristic of *Sarcosporidia*, as well as of other *Neosporidia*, that trophic growth and sporulation go on simultaneously, so that while pansporoblasts are continually forming, spores in different stages of maturation are to be seen at the same time. As the parasite develops it becomes surrounded by a capsule and appears as a sarcocyst between the muscle-fibers, containing pansporoblasts at the periphery and spores toward the interior, as previously described.

From the beginning the growth is more marked toward the periphery or at the poles, as the case may be, so that in time it becomes globular, oval (sarcocyst), or elongated, and forms the tubes of Rainey and Miescher.

Mechanism of Transmission.—The manner in which the virus is transmitted to another host is not well understood. Perrin has suggested that the transmission of the parasite occurs by means of the larvæ and imaginea of the blow-fly (*Calliphora*) or flesh-fly (*Sarcophaga*). Th. Smith and Negri have succeeded in infecting mice with *S. muris* by feeding them the flesh of infected mice, but this mode of transmission is not the same for other *Sarcosporidia*. Castellani's experiments on dogs gave negative results. A. J. Smith and Rivas failed to infect ducks

with *S. rileyi* by feeding experiments, and also by injecting the infected material under the skin, into the muscles, or intravenously.

Pathogenesis.—Sarcosporidiasis is a mild infection. The parasite is fairly well tolerated by the lower animals, but in cases of severe infection it may produce anemia and cachexia. In man the ingestion of parasitized and imperfectly cooked meat may give rise to abortive

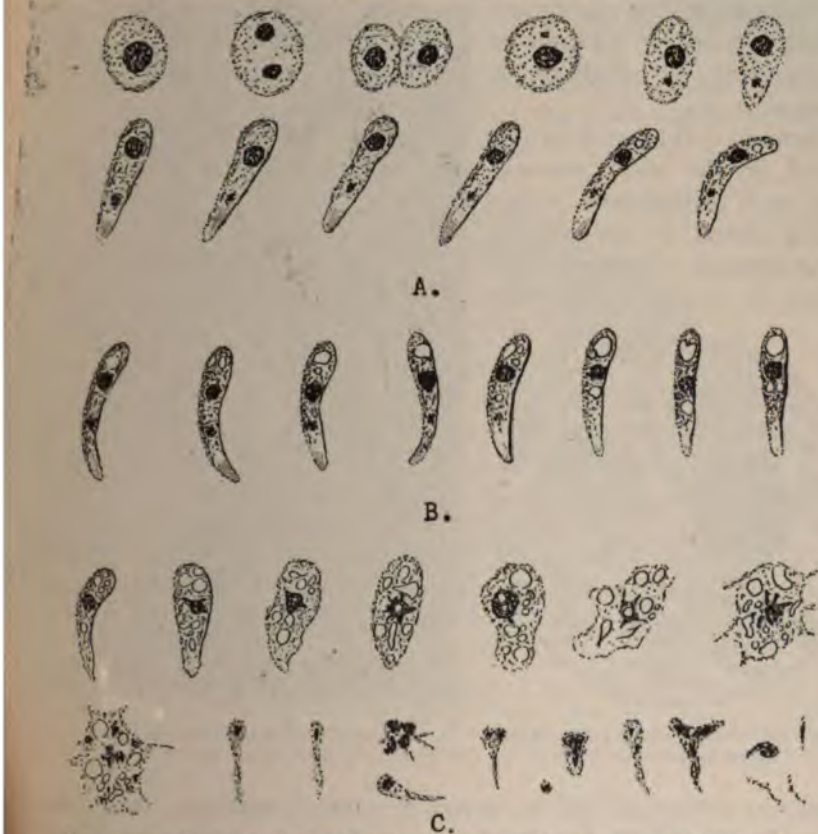


FIG. 87.—Sarcocystis rileyi. Drawing from contents of sporocyst showing developmental stages, degeneration and disintegration of spores. *a*, Mode of spore formation from cells of germinating layer. *b*, Various types of fully formed spores. *c*, Various degeneration and distintegration forms of spores.

symptoms, due probably to a toxic substance—*sarcocystin*—which is said to be present in the cyst. Three species have been found in man; *S. tenella*, *S. muris*, and *S. mucosa*.

1. **Sarcocystis Tenella** (Railliet, 1885).—This parasite is commonly found in the voluntary muscles of sheep and beeves, and is occasionally seen in the heart muscle of the latter in the form of small bundles, measuring about 500μ by 50 to 100μ. It has also been found in man; by Nancy, Vuillemin, and A. J. Smith.

2. **S. muris** (Blanchard, 1885).—This parasite is commonly found in rats. Baraban and Saint Remy have found it to be present in man.

3. **S. mucosa** (Blanchard, 1885).—Blanchard found this species in the kangaroo. It resembles *S. tenella*, and it is probable that this species, or one closely allied to it, belongs to the sarcocysts found in man by Kartulis in Africa and by Darling in Panama.

Several other species are found in the lower animals, such as **S. mischeriana** (Kuhn, 1865), found in the pig; **S. blanchardi** (Döflein, 1901) found in cattle; **S. bertrami** (Döflein, 1878), said to be found in man (Lindemann, Rosenberg, Kartulis, Koch); **S. hueti** (Blanchard, 1885) found in the seal; **S. kortei** (Castellani and Chalmers, 1909), in monkeys (Macacus); **S. rileyi** (Stiles, 1893), in the wild duck, etc.

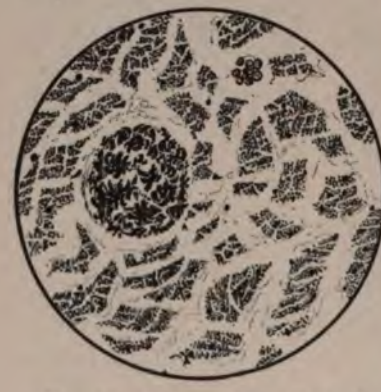


FIG. 88.—*Sarcocystis tenella* in the heart muscle of a cow.



FIG. 89.—Mouse infected with Sarcocystis muris.

IV. THE HAPLOSPORIDIA (Caulley and Mesnil, 1899)

The *Haplosporidia* are Neosporidia found as parasites in the intestine of marine annelides and in tumors of fishes. Morphologically they resemble Coccidia, and are closely allied to the Myxosporidia, from which they are differentiated by the absence of a polar capsule and the presence of a single nucleus in the spore. These parasites are characterized by the simplicity of their life history. The young

trophozoites appear as mononucleated or binucleated ameboid bodies, which eventually become encysted. They then increase in size, the nucleus divides, and a multinucleated schizont or *pansporoblast* is formed. Each nucleus now divides and gives rise to from 4 to 16 mononucleated *spores*, measuring 10 to 12μ in length by 6 to 7μ in width. The cyst finally ruptures, the spores are set free and develop into trophozoites by which the cycle is repeated. Sporogony is unknown.

Brumpt includes in the *Haplosporidia* a parasitic species found in man by Seeber in a polypoid growth of the nose—*Rhinosporidium*



FIG. 90.—Rhinosporidium seeberi. Section of a tumor showing proliferation of the epithelium (1 and 2) and the parasite in several stages of development. 3, Matured cyst; 4, rupture of the cyst with liberation of the pansporoblasts giving rise to a local cellular infiltration; 5, groups of young parasites. ($\times$ *about* 45. *After Seeber in Brumpt.*)

seeberi. This bears a close resemblance to the *Sarcosporidia*, except that it is found in the subcutaneous tissue and not between the muscle-fibers.

Rhinosporidium Seeberi (Wernicke, 1900).—This parasite was found by Seeber in Buenos Aires and by Kinealy and Nair in India, in cases of polyps of the nose. The organisms appear as minute dots or cysts, visible to the naked eye, and having an oval, round, tubular, or irregular shape. They were found below the epithelium or in subcutaneous hemorrhages, and also in the nasal discharge.

On section the cyst is found to be composed of a thin, striated cyst-wall, made up of an inner and outer coat containing either a mononucleated or a multinucleated mass of protoplasm (pansporoblast) in various stages of development. The size of the cyst varies from

10 to 30μ when young up to 0.2 to 0.3 mm. in diameter when full grown.

Life History.—The young trophozoite appears as an ameboid round body, provided with a single nucleus. As it grows the parasi becomes encysted, and by nuclear division gives rise to a multin cleated mass of cytoplasm *pansporoblasts* or *schizonts*. By rupture the cyst the pansporoblasts and spores are set free, and may eith set up an irritation or give rise to the formation of abscesses and di

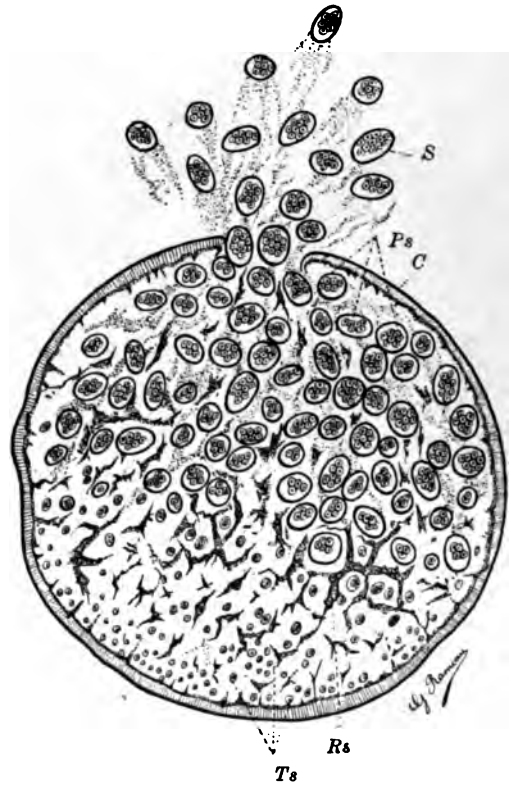


FIG. 91.—Evolution of Rhinosporidium seeberi. *s*, spores; *ps*, pansporoblast; *c*, cuticl *Rs*., residual mass; *Ts*., young pansporoblast. (*After J. B. Beattie in Brumpt.*)

charge externally; after which they degenerate and disappear grow into new parasites.

Mechanism of Transmission.—The mode of infection is not know The spores probably represent the infective phase of the parasit and may be transmitted to a new host directly or indirectly throug abrasions in the mucosa.

Pathogenicity.—This parasite believed to be the cause of polypoi growths or tumors of the nose and ears, which not uncommonly rec

after removal. The main lesion consists of proliferation of the nasal mucosa and submucosa, caused by the irritation set up by the parasite.

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CHAPTER IX

CILIATA (Ehrenberg)

Morphology and Structure: The Ectoplasm; The Cilia; The Nucleus.—Life History.—Classification.—Pathogenesis.—Parasitic Species Found in Man.

The Ciliata, a division of the Protozoa, also called Infusoria, are free-living or parasitic heterokaryota. They are characterized by the presence of a number of cilia on the surface of the body, which serve as organs of locomotion. They are commonly found in water, but may occasionally gain access to the alimentary canal of man and animals, where they multiply in such great numbers as to produce severe irritation and inflammation.

Morphology and Structure.—The Ciliata, of which the paramecium may be taken as a type, are characterized by having a distinct and constant shape. According to the species, they may be spheric, oval, or flattened. The body consists of an ectoplasm and an endoplasm, containing two or more nuclei, food and contractile vacuoles, pigment-granules, colorless granules, crystalline bodies, and undifferentiated particles. They are usually provided with a rudimentary mouth called a *cytostoma*. One species of Myctotherus has a *cytopyge*, or cell anus, but, as a rule, no definite opening exists and the undigested food is eliminated through any part of the ectoplasm.

The ectoplasm may consist of an undifferentiated and clear layer of cytoplasm, or it may be differentiated into three layers—an *outer thick layer*, a *middle* or *alveolar sheath*, which contains the myoneme threads arranged in vertical parallel lines, and an *internal layer*, which consists of a clear and transparent ectoplasmic substance. The cilia are attached to the ectoplasm.

The Cilia.—The cilia are hyaline, protoplasmic appendages, attached to the ectoplasm. They serve as organs of locomotion. Structurally a cilium resembles a flagellum, except that it is much smaller in size. Cilia take their origin from the nodes of the myoneme threads (alveolar layer), and project directly into the outer or hyaline layer of the ectoplasm. When properly stained and viewed under high magnification it will be seen that the cilia are actually connected with the nucleus by very fine achromatic threads. The cilia may appear as fine short whips, as thick processes known as *cirri*, or as a flat membrane or *plate*.

The Nucleus.—The Ciliata are provided with two kinds of nuclei—the *meganucleus* or *macronucleus* and the *micronucleus*. The former is

large in size, somatic, and trophic in function, whereas the latter is purely sexual and therefore not comparable to the kinetonucleus or the erroneously called micronucleus of the trypanosome.

The macronucleus is a distinct and prominent structure, consisting of an achromatic and a chromatic portion. It breaks down into granules before or after conjugation. The micronucleus is usually very small, and appears as a minute chromatic body in the center of an achromatic area.

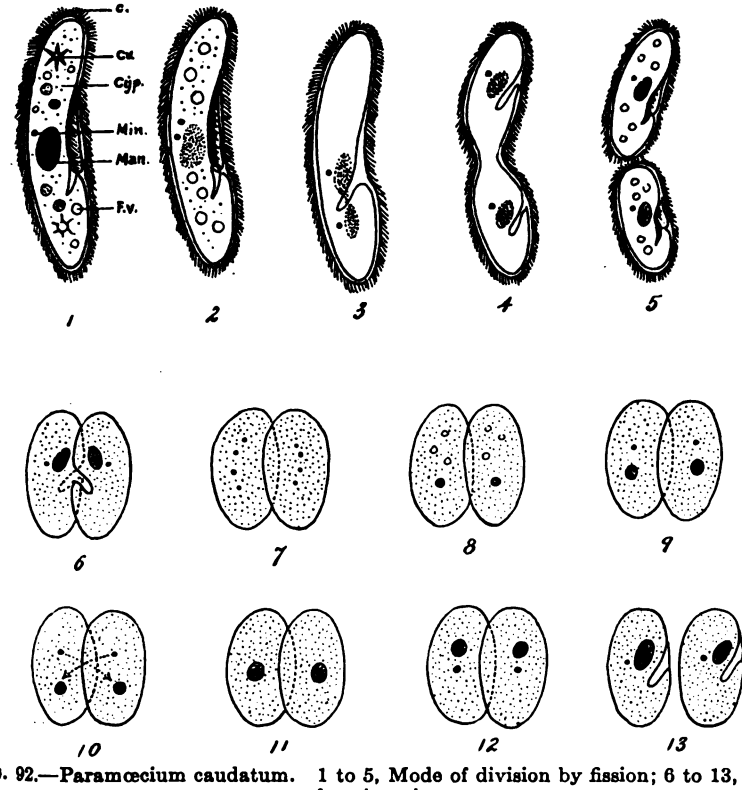


FIG. 92.—Paramœcium caudatum. 1 to 5, Mode of division by fission; 6 to 13, mode of conjugation.

Life History.—Reproduction takes place asexually, by fission, gemmation, encystment, or spore formation or sexually, after conjugation.

Fission.—Fission may take place by longitudinal or transverse division in the following ways: (1) Division of the cytostoma or gullet and formation of two mouths; (2) division of the micronucleus; (3) division of the macronucleus; and finally (4) division of the cytoplasm and formation and separation of the two individuals.

Encystment.—Encystment of the organism takes place, with the formation of several small individuals within the cyst.

Conjugation.—The normal course of conjugation or sexual reproduction as described in Paramecium requires from eighteen to thirty hours, according to the surroundings, and takes place as follows:

1. Two individuals meet and attach themselves by their anterior part and ventral surface, so that the cytostoma of each organism comes in contact. At first union is weak, but it in time becomes firm so that the individuals cannot be separated artificially without destroying one or both of them.

2. The macronucleus breaks up into numerous granules and disappears, whereas the micronucleus divides twice, forming two and then four nuclei respectively. Three of these, probably representing polar bodies, disappear, while one remains as the true spindle nucleus.

3. The spindle nucleus now divides unequally, forming one large nucleus—the *female* or *stationary nucleus*, and one small *male* or *wandering nucleus*.

4. Fertilization now takes place. This consists in the passage or exchange of the male nucleus of each cell into the other, which enters and fuses with the female nucleus of the other cell, so that each cell now contains a single fertilized nucleus or *synkaryon*.

5. The synkaryon or fertilized nucleus now divides unequally, forming a large nucleus, the *macronucleus*, and a small nucleus, the *micronucleus*. The two individuals now separate and become free.

Classification.—The classification of Ciliata is based upon the arrangement and differentiation of the cilia.

1. *Holotricha.*—These are motile Ciliata provided with cilia all over the body. The cilia are all of about equal length, and have no special oral cirri (*Chilodon, Colpoda, Uronema*).

2. *Heterotricha.*—These are motile Ciliata differentiated from the Holotricha by the presence of a row of cirri or membranellæ at the oral opening, forming a ring and inclosing a space—the peristoma (*Balantidium, Nyctotherus*).

3. *Hypotricha.*—Hypotricha are motile Ciliata deprived of cilia on the dorsal surface, and having cirri on the ventral surface. They are not known to be parasitic in man.

4. *Peritricha.*—These are Ciliata, having cilia in the adoral zone. They are not known to be parasitic in man.

Pathogenesis.—The Ciliata are uncommon parasites of man. *Balantidium coli* is found in the intestine, and is regarded as the cause of a special form of dysentery.

PARASITIC SPECIES FOUND IN MAN

Order	Genus	Species
Heterotricha	Balantidium	*B. coli* *B. minutum*
	Nyctotherus	*N. faba* *N. africanus* *N. giganteus*
Holotricha	Colpoda	*C. cucullus*
	Chilodon	*C. dentatus* *C. uncinatus*
	Uronema	*U. caudatum*

1. **Balantidium Coli** (Malmsten, 1857).—*Balantidium coli* is an infusorian of oval shape, somewhat pointed at one pole, and measuring from 30 to 200μ in length by 20 to 70μ in width. It is covered with cilia arranged in parallel rows, which give the parasite its characteristic striated appearance. The anterior pole is smaller than the posterior, and presents an oblique slit or groove, the *peristoma*, surrounded by numerous cilia (adoral cilia). The slit is continued by an infundibulum at the base of which is the mouth; a digestive tract, is, however, absent. The particles of food are incorporated in the endoplasm in the form of food vacuoles, as is the case in rhizopods, and the undigested food is eliminated through an anal aperture at the posterior pole which may be seen at the time of defecation or in stained preparations.

The *macronucleus* is either bean or kidney shaped, and near it is the *micronucleus* which is globular in shape. The endoplasm also contains contractile vacuoles, foreign bodies, and occasionally erythrocytes or other cells.

Habitat.—*Balantidium coli* is exclusively a parasite of the large intestine. This organism, it would seem, can live only in an alkaline medium. Normally it is found in the rectum of the hog, where it may become encysted, and in this condition be transmitted to man It is also found in the ourang-utang, macacus, and other monkeys.

Life History.—Reproduction takes place asexually by transverse division and conjugation. There is a preliminary encystment of two individuals, followed probably by fusion of the two cells and the final formation of two or more bodies (Fig. 93).

Encystment is marked by the parasite becoming globular in shape and the disappearance of the cilia. No specialized cyst-wall forms.

In the non-encysted form the parasite lives only a few hours outside of the host, but in the encysted stage it can resist unfavorable external conditions for a long time and even pass through the digestive tract without alteration. The non-encysted or motile forms are readily destroyed by gastric juice or by the secretions of the small intestine.

Mechanism of Infection.—The encysted form represents the infective stage in the life history of the parasite. These cysts are found normally in the rectum of the pig, and are carried to the digestive tract of man as the result of accident or carelessness. They may be transmitted to man through contaminated water, uncooked or underdone food,

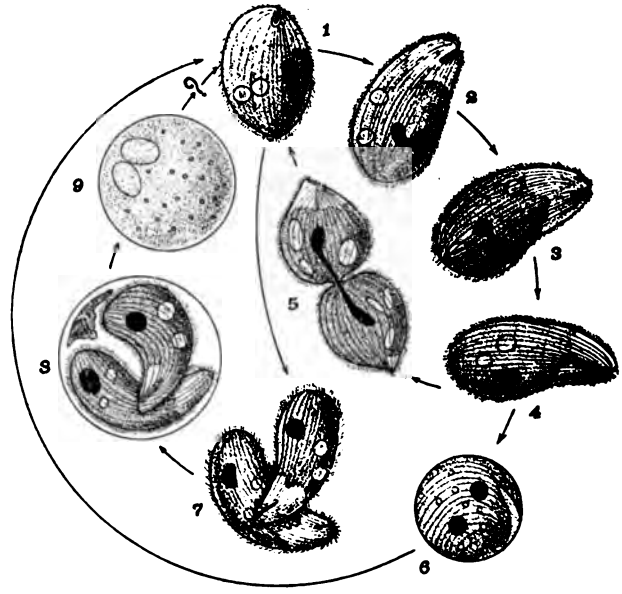


FIG. 93.—Reproduction of Balantidium coli: 1–5, Asexual reproduction by division; 6, encysted form of single individuals; 7, conjugation of two individuals; 8, reproductive cyst; 9, cyst with peculiar contents whose further development has not been followed. (*After Brumpt in McFarland.*)

etc. The cyst-wall is apparently capable of resisting the action of the gastric juice, but in passing through the intestine the cyst is dissolved, and on reaching the large intestine the parasite is set free and develops into a ciliated and motile organism in the rectum. Hogs are infected by swallowing the encysted forms. Auto-infection may also take place in man and in the lower animals.

Pathogenicity.—Malmsten found *Balantidium coli* in man in a case of cholera. Casagrandi and Barbagallo produced experimental enterocolitis in cats by giving them rectal injections of the parasite. Strong made a thorough investigation of balantidial enterocolitis in man in

the Philippine Islands and from his work we learned that the evolution of the parasite in the digestive tract of man gives rise to a distinct



FIG. 94.—Section of the large intestine of man from a case of balantidic dysentery showing the parasite (*Balantidium coli*) *P*, lodged in the submucosa *Sm*. (*From the collection of Joseph McFarland.*)



FIG. 95.—Section through an ulcer of the large intestine of man from a case of balantidic dysentery showing the parasite lodged in the submucosa at *A*, and in the lymph spaces at *B*.

type of dysentery. The mere presence of the parasite in the intestine of man does not, however, necessarily give rise to dysenteric symptoms.

Balantidic abscess of the liver may occasionally occur in balantidic dysentery.

2. **Balantidium minutum** (Schaudinn, 1899).—This parasite, closely allied to *Balantidium coli*, is differentiated from it by being much smaller in size (30 to 31μ by 14 to 20μ), and by the relatively large size of the peristome, which extends down to the middle of the body. It was found by Schaudinn in the intestine of a patient affected with malarial fever and enteritis. The symptoms were constipation alternating with diarrhea, abdominal pain, and gastro-intestinal derangement.

3. **Nyctotherus faba** (Schaudinn, 1899).—This parasite was found in the intestine of the same patient affected with *B. minutum*. The organism measures about 26 by 16μ, and is somewhat flattened. The peristome is deep, arched, and provided with cilia and cirri. The contractile vacuole is situated posteriorly, and there is a rudimentary anus, in the form of a slit on the surface of the organism, near it.

4. **Nyctotherus africanus** (Castellani, 1905).—This parasite is an hour-glass shaped organism, the anterior portion being smaller than the posterior. It measures about 45 by 35μ. The cilia are very small, and the cytoplasm is granular. The macronucleus is situated posteriorly, and near the contractile vacuole, and the micronucleus, which is very small, is adjacent to the macronucleus.

The parasite was found in the intestine of a patient suffering with sleeping sickness, associated with diarrhea alternating with constipation. The autopsy showed large numbers of the parasites in the cecum, congestion of the mucosa of the large intestine, but no ulcerations.

5. **Nyctotherus gigantus** (Krause, 1906).—This parasite was found in the intestines in conjunction with *Trichomonas intestinalis*. The organism has the shape of a truncated cone, and measures 90 to 400μ by 60 to 150μ. The macronucleus is large and bean shaped, and the micronucleus is round. Encysted forms may also be found in the feces.

6. **Colpoda cucullus** (Ehrenberg).—This organism is commonly found in sweet water. It is oval or bean shaped, and was found in the discharge from the intestine of a case of dysentery in man.

7. **Chilodon dentatum** (Dujardin, 1862).—The Chilodonta are somewhat flattened organisms showing a distinct convex or dorsal and a flat ventral surface, the latter containing the cilia. One species, *C. dentatum*, was found in the feces from a case of dysentery.

8. **Chilodon uncinatus** (Blochmann).—This organism is probably identical with *C. dentatum*. It was found by Manson in the feces of a case of schistosomiasis.

9. Uronema caudatum (Martini, 1910).—This organism is relatively small, measuring from 30 to 43μ by 11 to 15μ. It is bean shaped, and provided with cilia all over the body. It was found in a case of human dysentery in China.

With the exception of *Balantidium coli*, which is an obligatory parasite, either of man or animals, and which, as demonstrated by Strong, is the cause of a distinct type of dysentery in man, the other Ciliata just described are, as a rule, saprozoitic in habit, commonly found free in nature, and seen only as accidental parasites in man. They are, therefore, of secondary etiologic importance in diseases of the intestines. The fact that they have been found in conjunction with other parasitic diseases, such as dysentery, schistosomiasis, etc., is probably an indication that a previous change in the chemistry of the intestine is essential for their temporary adaptation to exist in the intestinal tract, and they are not, therefore, *per se*, true parasites of man.

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CHAPTER X

CHLAMYDOZOA—THE ULTRAMICROSCOPIC ORGANISMS AND FILTERABLE VIRUSES

I. CHLAMYDOZOA (Prowazek, 1909)

History. — Life History. — Classification. — Pathogenesis. — Parasitic Forms Found in Man: Neurorrhyctes hydrophobiæ; Cytoryctes variolæ; Cyclasterella scarlatinalis; Trachoma Bodies.

The Chlamydozoa are represented by a collective group of minute, protozoa-like parasites, commonly known as "cell-inclusion bodies," since they are usually found intracellularly. They may, however, occur in the free or extracellular state, when they are capable of passing through bacteriologic filters; hence the name "filterable virus" is also applied to them.

The intracellular organisms produce reactions in the host cell that are characterized by the production of a substance that envelops the parasite in a membrane or mantle (hence the name, chlamydozoa), thus forming a cell inclusion.

Morphologically, the cell inclusions consist of minute granules, 0.5 to 1μ in diameter, aggregated into oval, round or irregular bodies measuring 2 to 6μ. Stained by the Giemsa method, they appear as purple red bodies, inclosed in a bluish matrix—the mantle—inside of the cell.

History.—In 1907, Prowazek and Halberstaedter described such cell inclusions in the epithelial cells of the conjunctiva in cases of trachoma, and succeeded in inoculating them into anthropoid apes. Their results were confirmed by Greef.

Stargardt, in 1908, and Schmeichler, in 1909, found these bodies in cases of conjunctivitis neonatorum (non-gonorrheal), and since that time "inclusion blennorrhagia" has been differentiated from "gono-blennorrhea" by Linder.

Among other inclusion bodies may be mentioned those of epitheliosis desquamativa, found by Leber and Prowazek; those of swine pest, found by Uhlenhuth; those of sprue, described by Castellani; and likewise those of small-pox, scarlatina, molluscum contagiosum and hydrophobia (Negri bodies).

Life History.—In their simple form, the cell inclusions consist of minute masses of chromatin, known as "elementary bodies" (merozoites?). Inside of the cells, the elementary body grows and becomes the "initial body" (trophozoite?), which in time becomes surrounded

by a mantle and constitutes the "cell inclusion" (schizont?). The cell inclusions undergo fragmentation into a number of "initial corpuscles," which, by simple division, give rise to elementary bodies, and when these bodies enter a new cell the cycle is repeated.

Certain parasitic organisms found in pleuropneumonia of cattle and in diphtheria of birds, and regarded as Chlamydozoa, do not form cell inclusions, but remain as elementary bodies. In these bodies the life cycle consists in simple multiplication by fission, thus resembling bacteria.

Classification.—The Chlamydozoa are divided into two classes: I. *Chlamydozoa vera* and II. *Chlamydozoa strongyloplasmata.*

I. *Chlamydozoa vera.*—These have an "elementary body" and a "cell inclusion" stage. They are divided into three groups:

1. *Cytorrhyctes group,* the members of which cause destruction of the parasitized cells. They include the organisms found in vaccinia, variola, scarlatina, and hydrophobia.

2. *Cytovikon*(?) *group;* whose members cause proliferation of cells. In this group are included the bodies found in epitheliosis desquamativa and trachoma.

3. *"Gelbsucht" group,* which includes the organism found in "Gelbsucht" of the silkworm.

II. *Chlamydozoa strongyloplasmata.*—These are organisms that always remain as "elementary bodies." In this group belongs the organism found in pleuropneumonia of cattle and in diphtheria of birds, etc., known as "Filterable Viruses."

Pathogenesis.—The chlamydozoa are regarded as the cause of some important diseases of man, such as smallpox, vaccinia, trachoma, hydrophobia, scarlatina, etc.

PARASITIC FORMS FOUND IN MAN

1. **Neurorrhyctes Hydrophobiæ** (Calkins 1907).—*Neurorrhyctes hydrophobiæ,* commonly known as "Negri bodies," were discovered by Negri in 1903 in the ganglion-cells of the brain, especially in those of the *cornu ammonis* of animals suffering from hydrophobia. The bodies are round or oval in shape, and from 1 to 23μ in length. Some authorities regard these bodies as cell degeneration products, whereas others maintain that they are true parasites (Fig. 96).

Laboratory Diagnosis.—Although the earlier studies were made on sections, Williams and Lowden devised a simpler and more rapid means of diagnosis, *i.e.*, by the direct method of making stained spread preparations of the suspected material. The technic of this method is as follows:

(1) Place a bit of the gray matter on a clean slide; apply a cover-

glass, and press lightly upon it, so that the material will be spread in a fine layer.

(2) Slide the cover-glass gently along the slide, thus leaving a thin, even spread of the substance on the slide.

(3) Dry the spread in the air or by the aid of moderate heat, holding the slide at a safe distance from the flame.

(4) Stain with Giemsa solution.

Good results may be obtained by first fixing the preparation in equal parts of alcohol and ether for two minutes and then staining with diluted borax-methylene-blue.

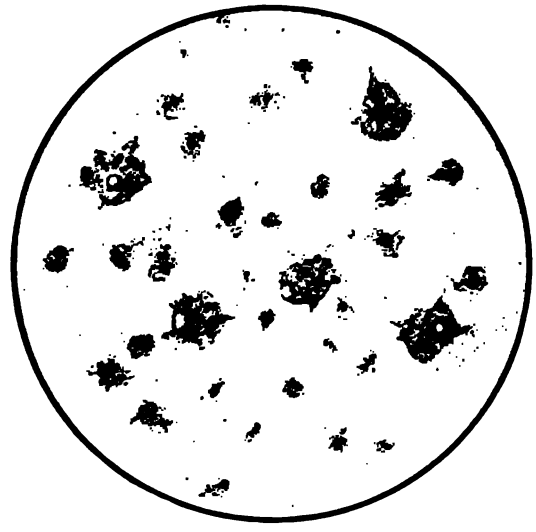


FIG. 96.—Negri bodies in spread from the brain.

When stained by the Giemsa method, the parasite appears inside of the cell as a bluish stained cytoplasm and a chromatic nucleus containing a central, red-stained body (the nucleolus?).

Artificial Culture.—Noguchi claims to have cultivated, from both "street" and "fixed" virus, very minute granular and dysmorphic, chromatoid bodies, which he regards as the causative agent of rabies. The method followed was similar to the one employed by him in the cultivation of the spirocheta of relapsing fever.

Mode of Transmission.—Hydrophobia is a common disease of dogs, the virus being present in the saliva of infected animals. The virus is transmitted from animal to animal by the act of biting. Certain animals, such as cats, rabbits, etc., are susceptible to the infection. Man may also be infected as the result of being bitten by an infected animal, or the virus may gain entrance through abrasions of the skin. It is believed that, as in tetanus, the virus reaches the central nervous

system more speedily by spreading along the nerve-fibers, than by passing through the circulation.

2. **Cytorrhyctes Variolæ** (Guarnieri, 1892).—Guarnieri described peculiar bodies found by him in the lesions of smallpox and in those produced by vaccination. Pfeiffer, Clarke, and Wasielewski confirmed Guarnieri's observations, and Councilman, Magrath, and Calkins published a full account of the life history of this parasite.

Morphology.—When very young, the *Cytorrhyctes variolæ* is seen in the epithelial cells as a very small chromatic body, measuring about 0.7μ. In older forms the parasite becomes ameboid and may attain a length of about 3μ, and when fully formed, up to from 10 to 14μ. In this stage the parasite may be seen to be made up of a cytoplasm and a nuclear substance, or chromatin granules (also called "protogonoplasm" (Calkins), distributed in minute spheric masses through the body, and lying in tiny vesicles that are liberated when the host cell disintegrates.

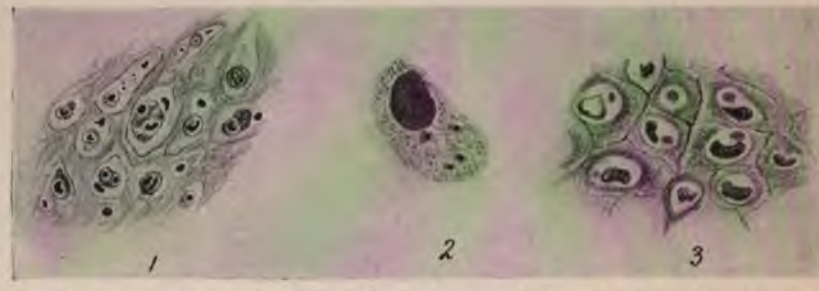


FIG. 97.—Vaccine bodies. 1, From a smallpox-pustule; 2 and 3 from the cornea of a rabbit inoculated with vaccine lymph. (*Slightly modified after Neuman and Mayer.*)

Life History.—As early as 1886 protozoa-like bodies were observed by Loeff and Pfeiffer in the lesions of smallpox. In 1892 Guarnieri observed similar bodies in lesions of the cornea of rabbits inoculated with vaccine lymph. These "vaccine bodies," which he called "*Cytorrhyctes vaccinæ*," were formed in the cytoplasm of the epithelial cells, but not in the nucleus. They were spheroid, oval, or irregular in shape, from 1 to 8μ in diameter, and exhibited ameboid movements.

Councilman, in 1903, claimed to have observed segmentation forms of these vaccine bodies with the formation of small, spore-like bodies measuring about 1μ. This observer also asserted that the presence of these bodies inside of the nucleus was a further stage in the life history of the parasite of smallpox. He believed that these intranuclear segments were derived from the spore-like bodies that have penetrated the nucleus. Calkins regards these bodies as protozoa belonging to the rhizopods.

Our present knowledge concerning the parasite of smallpox is, therefore, summed up in the statement that it is a protozoa belonging to the rhizopods; that it is found in the epithelial cells, either in the cytoplasm or in the nucleus, and that it reproduces by spore formation. The exact nature of these bodies, however, still lacks confirmation.

Bacteria are, of course, present in all the lesions of smallpox, and following vaccination. Although they may not have any specific etiologic significance, they nevertheless probably play an important part in the typical manifestation of the lesion.

3. **Cyclasterella scarlatinalis** (Mallory, 1904).—In 1904 Mallory described small round or elongated bodies which he found in the epithelial cells of persons suffering from scarlatina, and which he regarded as the cause of the disease.

These bodies are from 2 to 7 μ in length, stain deeply with methylene-blue, and are seen in association with radiate bodies composed of a central nucleus with several segments radiating from it. Although Field and Duval confirmed Mallory's observations, further research is necessary before the nature of these bodies can definitely be determined.

4. **Trachoma Bodies.**—In 1907 Halberstaedter and Prowazek and Greff described certain minute bodies found in the epithelial cells of the conjunctiva in the early stage of trachoma. These *trachoma granules* or *bodies* are seen as minute oval or coccoid grains of variable shape, grouped into masses close to the nucleus, and surrounded by a clear mantle—hence the name, *Chlamydozoa*, which has been applied to them.

When stained by the Giemsa method these trachoma bodies take on a reddish or a violet color, whereas the mantle is stained blue. They do not take the Gram stain. After some time these granules become less abundant and may disappear. The significance and nature of these trachoma bodies are not well understood at the present time.

II. THE ULTRAMICROSCOPIC ORGANISMS AND FILTERABLE VIRUSES

History.—Morphology and Structure.—Animal Inoculation.—Preparation of the Filtrate.—Culture.—Immunity.—Pathogenesis.—Filterable Viruses Peculiar to Man: Poliomyelitis; Typhus Fever.—Filterable Viruses Peculiar to Man and Animals: Foot and Mouth Disease; Pleuropneumonia of Cattle; Hog Cholera; Fowl Pest; Chicken Sarcoma. Filterable Viruses Peculiar to Plants; Mosaic Disease of Tobacco.—Conclusions.—Pseudoprotozoa.

The term ultramicroscopic organisms is applied to those imperfectly known forms of life whose size is so diminutive as to render them invisible under the microscope, even with the aid of optical appliances, and when viewed by direct illumination. Of these minute forms of life, a few probably belong to *Chlamydozoa vera*, more commonly known as "cell inclusions." These, as has been stated elsewhere, may be regarded as a collection of elementary bodies aggregated in a specialized form

inside of the cell. The majority of them, however, probably belong to forms that will always remain as "elementary bodies," being usually invisible and so minute as to be capable of passing through bacteriologic filters the pores of which are too small to permit the passage of ordinary bacteria.

History.—The existence of such ultramicroscopic forms of life had been suspected for many years, but this suspicion had never been confirmed until Loeffler and Frosch discovered, in 1898, that the virus of "foot and mouth disease" of cattle would pass through the finest porcelain filter and also that this filtrate, when inoculated into a healthy cow would transmit the disease. These authors proved further that the filtrate from the second animal would transmit the disease to a third, this again to a fourth, and so on indefinitely throughout a series of animals. Frosch and Rivas, in 1899, obtained identical results with "chicken pest."

Shortly after the discovery of Loeffler and Frosch, Beijernick demonstrated that the virus of the "mosaic disease" of the tobacco plant was also filterable. Some conception of the research work done along this line may be had from the number of diseases, about thirty in all, now known to be due to these ultramicroscopic forms of life.

The terms "filterable" and "ultramicroscopic" are often used synonymously; they do not necessarily mean that some filterable viruses cannot be rendered visible by the ordinary microscopic methods of illumination now employed. The virus of "pleuropneumonia" of cattle, for instance, can be seen by direct observation, using transmitted light, under a magnification of 1500 diameters.

Morphology and Structure.—Since our range of vision under the ordinary microscope is limited to 0.2 to 0.1 μ, and since the morphology of microscopic objects can be made out only indirectly with the aid of photographic plates, the possibility of studying these ultramicroscopic organisms by the direct method appears to be hopeless. Many improvements in optical instruments have been made within recent years, with the result that the ultramicroscope, or dark-field illumination, is now used extensively in laboratories. The principle of dark-field illumination is based on the fact that the rays of light are applied to the object in a direction horizontal to the long axis of the scope. By this method the object appears as a luminous point in the dark field, just as particles of dust are clearly seen in a sunbeam in an otherwise dark chamber. The delicacy of the adjustment is such that minute particles, scarcely larger than a protein molecule, can be detected, and repeated distillation in a silver vessel is required to obtain water that is free from particles that reflect light. This form of illumination is, therefore, of material advantage to us in our daily routine, for by its aid the larger ultramicroscopic organisms may be seen as minute bright

objects. They are not always, however, distinguishable from the inert particles of matter that are present in the liquids available for study.

Animal Inoculation.—Since these minute organisms cannot be rendered visible either with the microscope or by dark-field illumination, our studies must be based on the effects of filtrates when inoculated into susceptible animals. This method, while not entirely satisfactory, may nevertheless show the infectiousness and virulence of a virus. As in the case of pathogenic bacteria, the method forms one of the most important means for determining the etiologic factors in any disease.

A disadvantage in the inoculation of the filtrate is that, if the filtrate is of low virulence and of questionable transmissibility, as is the case with some pathogenic bacteria, the results are apt to be atypical, irregular, unsatisfactory, or negative. Another disadvantage lies in the fact that for the typical manifestation of the disease a symbiotic relation must probably exist between the ultramicroscopic organism and some bacterium, either the one or the other acting as the etiologic, predisposing, or concomitant factor, as the case may be. By means of filtration the bacteria are removed, which perhaps explains the failure to reproduce a typical manifestation of the disease in certain cases. As an illustration, hog cholera may be taken: *B. suipestifer* was originally regarded as the sole agent of the disease. It is now believed that the real cause is a filterable virus, and that the presence of the bacillus in question is concerned merely with certain manifestations of the disease, such as ulceration of the intestine, etc. It is probable that such symbiotic relations may also exist in yellow fever, the virus of which is responsible for the production of the early symptoms, whereas a secondary infection is the cause of the pronounced morbid changes that take place in the later phase of the disease (Smith, A. J.). The fact that after the third day of the disease mosquitos are no longer infected would tend to support this view. Finally, it is not improbable that the neglect to study these symbiotic relations in certain diseases may explain our imperfect knowledge of the etiology of typhus fever, dengue, beri-beri, pellagra, measles, scarlatina, etc.

Preparation of the Filtrate.—The method for preparing the filtrate consists in grinding the material to be examined—either an organ or a tissue—in a clean sterile mortar with a small quantity of clean sterile sand, after which it is suspended in a given amount of salt solution, and filtered through a Berkefeld or Chamberland filter. If the material to be examined is blood, then it should be allowed to coagulate, and the serum separated and filtered. All the apparatus used in the preparation of the filtrate should previously be cleaned and sterilized, and care should be taken to avoid any contamination of the filtrate

in subsequent manipulations. As a preliminary precaution it is recommended that the filtrate be first inoculated into ordinary culture-media and incubated at 37° C. for from twenty-four to forty-eight hours, under both aërobic and anaërobic conditions, in order to confirm the absence of bacteria from the filtrate.

Culture.—The virus of "pleuropneumonia" of cattle is visible, and appears as a very minute, spirocheta-like organism. It has been cultivated artificially.

The virus of fowl pest, fowl diphtheria, epithelioma contagiosum, Novy's rat disease, and poliomyelitis has also been cultivated. These organisms are, however, invisible, and their cultivation is marked by the fact that the subcultures are infective within reasonable limits of dilutions of the original.

Immunity.—It is characteristic of most of these filterable viruses that they confer a permanent immunity after the attack of the disease as is the case with yellow fever, typhus fever, scarlatina, etc.

Pathogenesis.—Among the diseases due to filterable viruses known at present, the greater number are peculiar to the lower animals; the next greater number are peculiar to man; then follow those common to man and the lower animals, and finally those peculiar to plants, of which only one variety, the "mosaic disease" of the tobacco plant, is known. Some of the most important and best known of these diseases are described below.

FILTERABLE VIRUSES PECULIAR TO MAN

1. **Yellow Fever.**—Yellow fever is an acute febrile infectious disease, characterized by marked blood destruction, jaundice and profound fatty changes of the internal organs, especially the liver. It is common in tropical America, especially in the West Indies and along the Gulf of Mexico.

Transmission.—The virus is transmitted by a mosquito, *Stegomyia* (*Aëdes*) *calopus*. In order to convey the infection the insect must bite the patient during the first three days of the disease, and an interval of twelve days is required for the infected mosquito to transmit the disease to man.

The Virus.—The virus passes through the Berkefeld and the Chamberland filter B. It is destroyed at 55° C. in ten minutes, and in forty-eight hours when exposed to the air at room temperature.

Noguchi and Pareja claim to have found a flagellate in the blood of yellow fever patients.

2. **Molluscum Contagiosum.**—Molluscum contagiosum is a local and infectious epithelial tumor of the skin, having a central colloid degeneration, hence the name "molluscum bodies" has also been

applied to the condition. The tumor can be squeezed out as a small, hard, white mass.

Transmission.—The virus is transmitted by contact, probably through an abrasion or a wound.

3. **Trachoma.**—Trachoma is a chronic follicular inflammation of of the conjunctiva.

Transmission.—The disease is transmitted by contact with discharges from similarly diseased conjunctivæ. Monkeys are susceptible to the infection.

The Virus.—The virus passes through a Berkefeld filter. The Koch-Weeks' bacillus is commonly found in the lesion, and for some time was regarded as its cause. It is possible that this bacterium bears a symbiotic relation to the infection.

4. **Poliomyelitis.**—Poliomyelitis, or "infantile paralysis," is an infectious disease, especially of children. It is characterized by fever, lesions of the central nervous system, and rapid atrophic paralysis of the voluntary muscles.

The Virus.—The virus is found chiefly in the central nervous system. It passes through the Berkefeld and Chamberland filters, and is inoculable in monkeys. The virus is destroyed in thirty minutes by a temperature of 45° to 50° C. and is easily destroyed by antiseptics.

5. **Typhus Fever.**—Typhus fever is an acute infectious disease characterized by fever, skin eruption, and marked prostration.

Transmission.—The virus is said to be transmitted by the body louse, *Pediculus vestimenti.*

The Virus.—The virus is usually found in the blood. It passes through a Berkefeld filter, and is inoculable in monkeys. It is destroyed at 52° C.

FILTERABLE VIRUSES PECULIAR TO MAN AND ANIMALS

"Foot and Mouth Disease."—Foot and mouth disease is an acute infectious disease of cattle communicable to man. It is characterized by high fever and the eruption of vesicles in the mouth and on the foot.

Transmission.—The virus is transmitted by contact.

The Virus.—The virus passes through the coarser porcelain filters and is destroyed at 50° C. in ten minutes.

Hydrophobia and **variola** are also peculiar to man and animals. Both have been described already. (See Chlamydozoa, pages 214–217.)

FILTERABLE VIRUSES PECULIAR TO ANIMALS

1. **Pleuropneumonia of Cattle.**—Pleuropneumonia or peripneumonia of cattle is an acute infectious disease, characterized by inflammation of the pleura and lung. The mortality is high.

Transmission.—The virus is transmitted by contact with the discharge from the lung.

The Virus.—The virus is found in the tissue affected. It passes through a Chamberland filter F, and is destroyed at 58° C. It has been cultivated artificially, and can be seen with the microscope under a magnification of 1500 diameters as a pleomorphic spira or coccoid body.

2. **Hog Cholera.**—Hog cholera is an acute contagious disease of the hog, characterized by fever, diarrhea, submucous and subcutaneous capillary hemorrhages, rapid emaciation, and ulcerations of the intestine.

Transmission.—The virus is transmitted by contact.

The Virus.—The virus is found in the blood; it passes through Chamberland filter F and B, and is destroyed at 60° to 70° C. in one hour.

In association with the infection, *Bacillus suipestifer* is found in the lesion. For years this organism was considered the sole cause of hog cholera, but it is now regarded as a secondary source of infection. It is probable that this bacillus bears an important symbiotic relation to the disease.

3. **Fowl Pest.**—Fowl pest is a disease of chickens, pheasants, and sparrows. It is characterized by a bloody diarrhea and a high mortality.

Transmission.—The virus is transmitted through the feces and nasal secretions of infected birds.

The Virus.—The virus invades the entire body—internal organs, nervous system, the blood, etc. It is filterable through a Chamberland filter, and is destroyed at 55° to 60° C. in thirty minutes. Cell inclusions, found in the brain and measuring 1 to 1.5μ, have been described.

4. **Chicken Sarcoma.**—Chicken sarcoma is a malignant growth resembling a spindle-cell sarcoma.

Transmission.—The tumor is transmitted to one strain of fowl only.

The Virus.—The virus passes through a Berkefeld filter and is destroyed at 50° to 55° C. in fifteen minutes.

In order to transmit the disease the filtrate must be introduced well within the tissue, and apparently the part to be inoculated should previously be traumatized in order to secure a positive result. In this respect the virus of chicken sarcoma resembles the spore of the tetanus bacillus.

FILTERABLE VIRUSES PECULIAR TO PLANTS

Mosaic Disease of Tobacco.—The mosaic disease of tobacco plant is characterized by the appearance of peculiar patches on the leaves, that somewhat resemble mosaic work in arrangement and distribution.

Transmission.—The disease is transmitted by contact or through the air.

The Virus.—The virus is found in the lesion, and is very resistant to drying and heat. It requires a temperature of 70° to 80° C. or two years at room temperature to be destroyed, and resists the action of 95 per cent. alcohol for ten minutes.

CONCLUSIONS

The following is a résumé as to the most salient biologic features of the ultramicroscopic organisms or filterable viruses:

1. One group of organisms, such as yellow fever, typhus fever, and perhaps poliomyelitis, commonly regarded as blood diseases, require an intermediate host—a biting insect—for their transmission. This suggests that these viruses are probably protozoan in nature. Another group is transmitted by contact (pleuropeneumonia, fowl pest, etc.) or through abrasions in the skin (hydrophobia, molluscum contagiosum, chicken sarcoma, etc.). These may or may not be protozoan in nature.

2. Cultures *in vitro* have been grown successfully only in the case of pleuropneumonia of cattle, fowl pest, and poliomyelitis (Flexner and Noguchi).

3. With the exception of the virus of mosaic diseases of the tobacco plant, the other viruses are destroyed at a much lower temperature than bacteria.

4. As to the after-effect of the diseases produced by these minute organisms, it may be said that in most instances immunity is complete and of long duration. This is true of such diseases as yellow fever, smallpox, scarlet fever, typhus fever, etc., in which a second infection is the exception, but passive immunity as a rule, has not been obtained.

5. Finally it is probable that when the nature of these ultramicroscopic organisms is better understood, our conception of living matter will be changed, and we shall cease to differentiate between animal and plant forms.

Since these organisms are so minute as to be capable of passing through the finest filter, and since they cannot be precipitated even by centrifugalization with the most powerful machine, it would seem that some of their properties must be due to the very minuteness, and as in the case of colloidal substances or the enzymes, their action may be regarded as a physical phenomenon.

PSEUDOPROTOZOA

It is often difficult, in prepared sections, to determine with certainty the nature of certain objects or bodies that bear a close

resemblance to the protozoa. It is essential, therefore, that observations be made upon fresh material and upon preserved material at the same time.

Instances have been known in which the product of cell degeneration or the degenerated cells themselves have been mistaken for parasites. In the cells of metazoa peculiar forms are not uncommonly seen that are easily mistaken for protozoa; this is true particularly of amebas and sporozoa. Literature is replete with descriptions of many protozoa-like bodies that were observed in cases of pernicious anemia, various skin diseases, numerous diseases of the lower animals, tumors, etc. There is not, however, sufficient evidence of the true microörganismal nature of these bodies to enable them to be classed among the protozoa.

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PART III

METAZOA

CHAPTER XI

GENERAL CONSIDERATION OF METAZOAN PARASITES

Morphology and Structure.—Life History.—Habitat.—Erratic Parasites.—Mechanism of Transmission.—Pathogenesis.—Effect of the Parasite Upon the Host.—Prophylaxis.—Termination of Parasitic Infestation.—Classification.

A metazoan is a multicellular animal, either free living or parasitic in habit. It is characterized by a cell differentiation of the soma and division of labor. In the course of their development all metazoa undergo metamorphosis more or less complete and which consists in the primary segmentation of a true egg or ovum, and the subsequent passage through an embryonic development in which at least two distinct germinal layers are differentiated. With the exception of the cestodes and a few other parasitic species, also the extremely modified forms of males, all metazoa have a permanent digestive tract and a sexual differentiation is the rule. Parasitic metazoa may be ectoparasites (for example, many species of insects) or endoparasites (many vermes).

Morphology and Structure.—All metazoan parasites have a distinct and constant shape. This is either flat (trematodes and cestodes) or cylindrie (nematodes). The body is differentiated into an anterior or cephalic and a posterior or caudal end, and it exhibits a distinct symmetry. Structurally, most metazoan parasites are provided with distinct organs of reproduction, digestion, respiration, and circulation, and they possess a more or less specialized nervous system.

Life History.—Metazoan parasites have a complicated life history. Most of them have an indirect development and require an intermediate host, in which they undergo profound changes and metamorphoses prior to their successful entrance and maintenance in a new host. Others have a direct development and require only one host. An alternation of generation is the rule, and the intermediate host may be an invertebrate (trematodes and some nematodes) or a vertebrate (cestodes and some nematodes). Parasitic metazoa may be ectoparasites, as, for example, most of the insects; or endoparasites, as, for example, the cestodes, trematodes, etc. They may be temporary parasites (mosquitos), periodic parasites (ticks), or permanent parasites (lice, worms, etc.).

Habitat.—In general, the parasitic metazoa in man are divided into two classes—ectoparasites and endoparasites. The ectoparasites inhabit the surface of the body or the easily accessible normal cavities, such as the nose, ear, and mouth. The endoparasites inhabit the internal cavities, the subcutaneous tissue, the internal organs, or the blood. Generally speaking, every parasite develops by preference in certain organs or tissues of the body, or may become attached to certain regions of the intestine; thus Ankylostoma and Trichinella live in the upper part of the small intestine, whereas Trichocephalus inhabits the cecum. This is not a matter of chance, but is dependent on the physicochemical condition of the part, which is confirmed by the fact that failure of the organism to reach the part, or its experimental transplantation to another region, usually results in death of the parasite.

Erratic Parasites.—The term *erratic* is applied to those parasites that, under certain conditions, may be found in abnormal localities; thus *Fasciola hepatica* may be found in the lung; *Paragonimus westermanii*, in the liver; Ascaris, in the peritoneal cavity, etc.; but any parasite may become erratic when the physicochemical condition of the part of the body involved is so altered as to furnish a favorable medium for its development in other localities; this usually occurs in cases of pronounced infestation or when complicated with other diseases.

Mechanism of Transmission.—For transmission to another animal those metazoan parasites having an indirect development require an intermediate host; this may be either an invertebrate (Filaria and Trematoda) or a vertebrate (Trichinella and Cestoda). In metazoa having a direct development the transmission is direct (as is the case in many nematodes). In either case the parasite usually undergoes preparatory changes or metamorphosis outside of the host. These preparatory changes may consist merely in the development of a larva inside of the egg (Ascaris, Trichocephalus), of a free larva (Ankylostoma), or of an oncosphere or encysted larva (cestodes), or the parasite may undergo profound metamorphosis (trematodes). In general, all thick-shelled egg nematodes are transmitted in the larva egg stage (Ascaris, Trichocephalus); all thin-shelled eggs are transmitted in the free larval stage (Ankylostoma), and filarias in the larval stage, as found in the invertebrate host; all cestodes are transmitted to man either in the oncosphere (*Tenia echinococcus*) or bladder-worm stage (*T. satinata*), and all trematodes in the free encysted larval stage. Most insects are ectoparasites and are transmitted directly in either the larval or the adult stage.

Pathogenesis.—The metazoan parasites are the cause of important diseases in man, such as filariasis, trichiniasis, etc. As a rule, these

diseases are marked by slow onset, run a chronic course, and have an uncertain termination. The mere presence of the parasite is often of no especial consequence to the host unless it is lodged in a vital organ, in which case the mechanical action of the parasite may prove fatal, *e.g.* (*Cysticercus cerebralis*). In other instances the parasite may be the source of chronic irritation or inflammation, leading to destruction of tissue and ulceration, which in turn predispose to bacterial infection and not uncommonly are the source of grave complications. Few insects may be said to be the cause of diseases of man (Pediculus, Sarcoptes, etc.), but, on the other hand, a large number of insects are transmitters of important diseases.

Effect of the Parasite Upon the Host.—The effect of metazoan parasites upon the host is dependent upon many factors, such as the species of parasite; the number present; their location and migration; abstraction of food; production of toxin; condition of the host, and complications, with especial reference to bacterial infection.

Although certain organisms, as, for example, Filaria, Ascaris, and other intestinal parasites, may exist in the host without producing any apparent ill effects, beyond a moderate degree of anemia and eosinophilia, others, such as Ankylostoma, usually produce severe anemia and other grave disturbances.

The location of the parasite plays an important part in parasitic disease; thus ascarides in the intestine are relatively harmless, but when lodged in the pancreatic duct, gall-bladder, or appendix, etc. they may give rise to grave symptoms, and cysticercus in the brain usually proves fatal.

In their migration, the Ankylostoma larvæ on entering the skin produce dermatitis (coolie itch), and may be a source of bacterial infection. The penetration of the intestinal mucosa by the larvæ of Trichinella is the source of gastro-intestinal disturbance, and their wandering through the body, previous to becoming encysted in the muscle, is probably responsible to a large extent for the subsequent acute symptoms of trichiniasis.

The quantity of food appropriated by the parasites is undoubtedly an important factor, especially in children during the period of active growth. Leuckart has determined that *Dibothricephalus latus* gives off proglottides to the weight of 140 grams in one year; *Tenia saginata*, 550 grams, and *Ascaris lumbricoides*, 42 grams of eggs in the same period. Undoubtedly a large amount of food material is consumed to sustain this growth, and this perhaps explains the voracious appetite sometimes manifested by the patient in some parasitic infestations. The condition of the host is another important factor in parasitic diseases, for although ascarides may be relatively harmless in a healthy intestine, when enteritis and ulceration are present they may produce

perforation and peritonitis. Any disease that diminishes the natural resisting power of the organism tends to aggravate a parasitic infestation.

The effect of toxins liberated by the parasite upon the host, as a rule, is of secondary importance.

As has been stated, bacterial infection plays a very important rôle in parasitic disease; thus Trichocephalus and Ascaris may predispose to appendicitis. The fevers often found in cases of uncinariasis, schistosomiasis, paragonomiasis, etc., are probably caused by bacteria entering the body through the wounds inflicted by the parasite, which not uncommonly are the source of fatal complications.

Prophylaxis.—For the prevention of metazoan infestation it is essential that the hygienist possess a fair knowledge of the life history and mode of transmission of the parasites. Most organisms are introduced into the system either directly or indirectly, as with the food or drinking water. Consequently the proper cooking of meats and vegetables; the boiling of suspected water; the purification of the water supply of a community and the proper cooking of food in general, should receive first consideration. In this way a large number of the parasitic infections—as by the nematodes, the trematodes, and the cestodes—can be avoided. For the prevention of the development of such parasitic nematodes as Filaria, which is transmitted by the mosquito, care should be taken to avoid the bite of this insect. In the prophylaxis of uncinariasis it is of great importance properly to disinfect the soil, stagnant water, and excreta in mining districts, and to see that the hands are *thoroughly washed before meals*. As the Ankylostoma larvæ also penetrate the skin, the wearing of proper shoes and gloves is to be recommended. A general education of the laity as to the principles of hygiene in general, and of personal hygiene in particular, is a valuable aid in preventing the development of parasitic diseases and considerably facilitates the difficult task of the hygienist.

The parasitologist should bear in mind that an individual infested with some parasite in which a positive diagnosis has been made is less dangerous to the community than is the apparently healthy person, who exhibits no clinical manifestations of the disease, since these ambulatory cases are not likely to be affected by hygienic and prophylactic regulation. Insects, which are the carriers of important diseases in man should be destroyed in either the larva or the adult stage, and screening of the house should not be neglected.

Termination of Parasitic Infestation.—As has been stated in Chapter II, a parasite may disappear from the host in one of three ways: by medication, by spontaneous expulsion, or by actual death of the parasite. Spontaneous expulsion of those parasites directly or indirectly exposed to outside influences is not uncommonly seen in the

course of infectious fevers. Thus ascarides, tapeworms, and other intestinal parasites are often passed with the stools in the course of an acute attack of infectious fevers, such as measles, scarlatina, typhoid, smallpox, or even during the febrile period following vaccination. This, of course, is not due to the fact that the infectious disease in question (smallpox, typhoid, etc.) has any specific antagonistic action on the parasite, but rather to the increase in the body temperature to 103° F., or higher. The abnormal temperature, to which the parasite is unaccustomed, probably leads it to detach itself from the mucous membrane of the intestine, and it is finally expelled by the intestinal peristalsis.

The natural death of a parasite probably occurs much earlier than is generally supposed. Thus, it is known that the male Trichinella lives only a few weeks and the females not over three months. Judging by the rarity of ascarides in children over ten years of age, as compared with those who are younger, the life of *Ascaris lumbricoides* is probably not over from four to six years, and that of *Ascaris canis* in dogs is probably less. The life of the hookworm has been calculated to be about six years. The writer had the opportunity of examining in Philadelphia a patient infested for the last five years with *Schistosoma japonicum* and another infested with *Filaria loa*, both patients having returned from a missionary trip to the Orient, where the disease was contracted. These patients have improved steadily to a point where the microfilaria have become less and less numerous in the blood of the one patient, and the eggs of the Schistosoma have almost disappeared from the feces of the other. This would point to the fact that the life of these two parasites is probably less, and perhaps not more, than six or ten years. Concerning *Filaria bancrofti*, microfilaria were found six years ago in the blood of a young Porto Rican. This patient has been a student in the Law School of the University of Pennsylvania for the last four years, and consequently here in the North has not been exposed to reinfection. When seen by the writer, after this time, the patient was suffering from lymphangitis of the left leg, but in spite of repeated examinations of the blood, made at different hours of the day and night, no microfilaria were found. This would seem to indicate either that the adult females had died, or that, if still alive, they were in the last stages of their existence, reproducing but few microfilariæ—too few in number to be detected in the peripheral blood. This would point to the fact that the life of *Filaria bancrofti* is not much over six and perhaps less than ten years.

The disappearance of the parasite from the body, however, does not necessarily imply that other symptoms due to complications, will also disappear. Thus, in elephantiasis, microfilaria are often absent

from the blood. This is true also of chronic cellulitis and fibrous adenitis in chronic filariasis.

Classification.—The metazoan parasites of man may be arranged in the following groups:

1. Platyhelminthes.
2. Nemathelminthes.
3. Annulata.
4. Arthropoda.

1. *The Platyhelminthes.*—The Platyhelminthes are flat worms, bilaterally symmetric. The body is oval or leaf shaped, or tape like, and has no true celomic cavity. The surface may be covered with a ciliated epithelium, as in free-living Turbellaria, or with a cuticle, as in Trematoda and Cestoda. The alimentary canal may be entirely absent (Cestoda) or incomplete, consisting only of mouth and a forked intestine, without an anal aperture, commonly called *cecum* (Trematoda). The excretory system consists of a bilateral nephridium system, which begins in the flame cells, *i.e.*, ameboid cells provided with a lash of cilia, and continued by a series of fine channels or capillaries that anastomose to form two lateral canals, ending posteriorly either in a common duct (Trematoda) or in two excretory ducts. The nervous system consists of two cerebral ganglia and nerves.

The Platyhelminthes are all hermaphroditic, with the exception of Schistosoma in which the sexes are separate. The ova are generated in the ovary, near which they are fertilized, and receive food (yolk) from the yolk or vitelline gland through the vitelline duct. Their covering or shell is supplied by the secretion of the shell gland before they enter the uterus, where they remain until they are passed to the exterior. The male organs consist of testis, vasa deferentia, vesiculæ seminales, cirrus or penis, and occasionally a cirrus pouch. The Platyhelminthes are divided into:

Class I. *Turbellaria.*—Free-living flat worms; body covered with cilia; alimentary canal incomplete; no anus.

Class II. *Nemertea.*—By some regarded more nearly related to annelids are free living worms; alimentary canal complete.

Class III. *Trematoda.*—Parasitic flat worms with incomplete alimentary canal; body not segmented.

Class IV. *Cestodaria.*—Body not segmented, like the trematodes; alimentary canal absent.

Class V. *Cestoda.*—Parasitic flat worms having no alimentary canal; body segmented.

Of those mentioned, only the trematodes and cestodes are of importance in human parasitology.

2. *Nemathelminthes.*—The Nemathelminthes are worm-like metazoa, round and filiform in shape, non-segmented, but covered with a ringed cuticle. The alimentary canal is usually complete, and con-

sists of a mouth, an intestine, and an anal aperture. The sexes are divided. The Nemathelminthes are usually parasitic at some period in their life history. They are characterized by an almost complete absence of cilia. These parasites are of great importance in human parasitology, for they include such species as *Ankylostoma duodenale, Filaria, Trichinella spiralis*, etc., which are the cause of serious diseases in man.

3. *Annulata.*—The Annulata, or Annelides, are metazoa having elongated bodies, divided externally into a number of rings that represent a division of the internal parts into segments, *somites*, or, as they are also called, *metameres*. They usually have a large celom. The nervous system consists of a cerebral ganglion, with double commissure and ventral cord. The excretory organs are represented by metamerically arranged pairs of nephridia that open at the side of the body. The Annelides are usually hermaphroditic, and comprise several classes, but only the Hirudinea or Discophora, *i.e.*, the leeches, are of importance in human parasitology.

4. *Arthropoda.*—The Arthropoda are bilaterally symmetric organisms, the body being composed of more or less differentiated segments, and covered with a chitinous cuticle or skeleton. Behind the mouth one or more pairs of appendages are densely chitinized and turned inward, and serve as jaws. They are divided into four classes:

Class I. *Crustacea.*—These are aquatic arthropods; respiration occurs by means of gills; two pairs of antennæ are present.

Class II. *Arachnida.*—These are terrestrial arthropods; respiration takes place through the trachea or cutanea. The body is generally divided into two parts: the anterior or *cephalothorax* (head and thorax fused), which comprises the mouth parts and four pairs of legs; the posterior part, or abdomen, may or may not be articulated. The group contains several orders, of which only the *Linguatulida* and *Acarina* are of importance in human parasitology.

Class III. *Miriapoda.*—These parasites have an elongated body and are provided with numerous pairs of legs; respiration takes place cutaneously; one pair of antennæ are present. According to the arrangement of a pair of legs on each segment, the parasites are divided into—(1) Diplopodes or Chilognathes, with two pairs of legs to each ring, and (2) Chilopodes, with one pair of legs to each ring.

Class IV. *Hexapoda or Insecta.*—Arthropoda that are characterized by having three pairs of legs, the body being divided into three distinct parts: head, thorax and abdomen. The head is provided with antennæ, the thorax, usually with two pairs of wings, and the abdomen is generally composed of nine visible segments. The insecta are of great importance in human parasitology. The arthropods also comprise the class Onchophora (Lankester), which includes the genus Peripatus, which is of no importance in human parasitology.

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CHAPTER XII

TREMATODA

GENERAL CONSIDERATION OF PARASITIC TREMATODES

History.—Morphology and Structure.—Mode of Fixation.—Life History.—Mechanism of Transmission.—Habitat.—Pathogenesis.—Diagnosis.—Treatment and Prophylaxis.—Classification.

The trematodes are commonly flat, leaf-like, non-segmented organisms. They are exclusively parasitic, living on the exterior (skin or gilletes) (ectoparasites); or in the interior (alimentary canal, etc.) of the host (endoparasites). Structurally the trematodes are closely related to the free-living, triclad Turbellaria, from which they are probably derived. They are distinguished from the latter by certain characteristics developed as a result of their parasitic adaptation. Thus the adult trematodes have lost their cilia, which are present only in the aquatic larval stage, and are armed with specialized cuticular organs (suckers) for attachment to the host. Other features common to them are the atrophy of sense organs in general and the tendency to develop accessory ganglia near the suckers; the disappearance of eye spots, which are only occasionally seen, either in the adult or in the larval stage (miracidium) of some ectoparasites; the incomplete alimentary tract (absence of anal aperture), and the greatly specialized genital organs, which fill a large part of the body.

History.—Our knowledge of the trematodes began with the discovery of the liver fluke by Jehan de Brie, in 1379. Gabucinus, in 1547, also described these parasites, but it was not until 1777 that Müller gave an accurate idea of the form of the organisms. Zeder, in 1800, termed them "sucking worms," and Rudolphi, in 1808, suggested the name "Trematodes," *i.e.*, "pierced by holes." From this time on several important contributions appeared upon the study of the parasites, such as the observations of Laurer in 1830 (the canal he discovered bearing his name); those of Van Beneden in 1858; and of Leuckart in 1867, who divided them into Distoma and Polystoma; the writings of Thomas in 1883, who elaborated the life history of *Fasciola hepatica*. In 1892 Monticelli revived the old classification of Burmeister, which recognized three orders: Heterocotylea, Aspidocotylea, and Malacocotylea.

Morphology and Structure.—The trematodes are generally leaf-like or tongue-shaped, but rarely cylindric. The presence of one,

two, or more suckers is characteristic of this group. None of the parasitic species found in man bear more than two suckers; one is situated anteriorly, and called the *oral sucker*, and one is placed ventrally, and termed the *ventral sucker*, or *acetabulum;* the latter is usually situated at the anterior third of the body or close to the oral sucker. In a few species the acetabulum is situated at the posterior part of the body. The Monostomidæ have but one sucker.

The Cuticle.—These parasites are covered with a soft or chitinous-like cuticle, which in some cases, as in *Paragonimus westermanii*, is

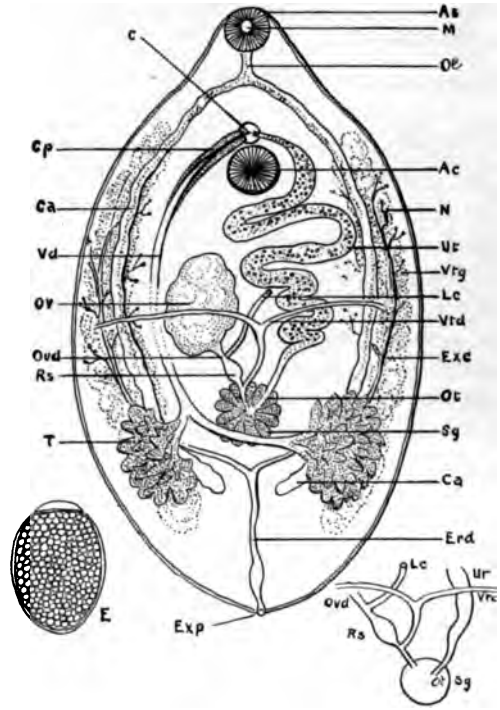


FIG. 98.—Diagram of the anatomy of a trematode. *As*, anterior sucker; *Ac*, acetabulum; *M*, mouth; *Oe*, oesophagus; *Ca*, ceca; *N*, nephridium; *Exc*, excretory canal; *Exd*, excretory duct; *Exp*. excretory pore; *Vtg*, vitelline glands; *Vtd*, vitelline duct; *Sg*, shell gland; *C*, cirrus; *Cp*, cirrus pouch; *Vd*, was deferens; *T*, testes; *Ov*, ovary; *Ovd*, oviduct; *ot*, oötype; *Rs*, receptaculum seminis; *Lc*, Laurer's canal; *E*, egg.

provided with spicules. The difference in structure of the cuticle is of importance, as it serves as a means of determining the species. Next to the cuticle is the subcuticle, which appears as a velvety layer made of numerous delicate fibers.

The Muscular System.—This is situated below the cuticle, and is made up of circular, longitudinal, dorsoventral, and diagonal fibers. The body is divided into an outer zone or cortex and an internal zone or medulla. The cortex is comprised of the cuticle and muscular

system, while the medulla consists of mesenchyme and connective-tissue-like cells which represent the supporting framework containing the internal organs.

The Digestive Tract.—The digestive tract is incomplete, ending in a culdesac or cecum, having no anal aperture. It consists of a mouth, situated at the oral sucker, and a pharynx, which may or may not have lateral pouches. The esophagus may be short or long, with or without sphincter muscles, and is often provided with unicellular salivary glands. The intestine generally consists of two blind tubes, which are usually simple, but may be branched (*F. hepatica*) or may anastomose (Schistosoma).

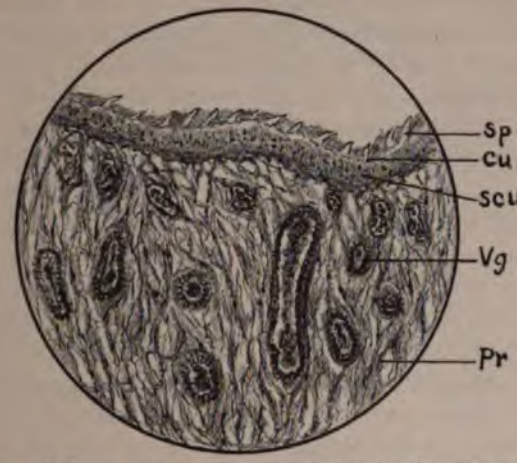


FIG. 99.—Section of Paragonimus westermanii showing *Sp*, spines; *Cu*, cuticle; *Scu*, subcuticle; *Vg*, vitelline glands; *Pr*, parenchyma.

The Nervous System.—This is usually rudimentary, and has not been observed in all species. Generally it consists of two cerebral ganglia, united by a transverse commissure and two nerve cords, one from each ganglion.

The circulatory and respiratory systems are absent.

The Excretory System.—The excretory system is well developed, and consists of a nephridial system, which begins in special ciliated cells called "flame cells," which communicate with fine *excretory capillaries.* These capillaries open into *primary collecting canals* that anastomose freely and then join the *excretory canals.* The latter are two in number, and are situated laterally at each side of the medullary portion of the body. These canals then join at the middle of the body to form the *common collecting* duct, which opens into an *excretory vesicle* and finally empties dorsally, either posteriorly, below or at the level of the acetabulum. The study of the flame cells can easily be made on the free-living Turbellaria (Planaria) and Rotifera.

The Reproductive Organs.—The trematodes, with the single exception of the Schistosoma, are hermaphrodites. The male organs consist of the testis, usually two in number, and situated posteriorly to the ovary; in a few instances (*Dicrococlium lanceatum*) they are situated anteriorly to this organ. Each testicle is provided with a *vas deferens*, which unites anteriorly into a common duct and ends in a cirrus or penis at the genital opening, which is usually situated near the acetabulum and anteriorly to it. In some instances, as in *Fasciolopsis buski*, the cirrus is inclosed in a muscular pouch provided with glands; this is called the *cirrus pouch* or prostate. In certain genera, such as Fasciola, Clonorchis, etc., the vas deferens, in its course, shows a small dilatation—the *vesicula seminalis*.

The female reproductive organs present a more complicated arrangement, and consist of essential and secondary or accessory parts. The essential parts are the ovary, the oviduct, the oötype, and the uterus. The accessory parts consist of the *receptaculum seminis*, the *vitelline glands*, the *vitelline ducts*, the *shell gland*, and, in addition, a small canal (*Laurer's canal*). The *ovary* is single, relatively small and oval in shape, although sometimes it is irregular or branched, and is usually situated anteriorly to the testis. The *oviduct* is short and receives the vitelline ducts; before uniting with the uterus it is surrounded by the shell gland. The *oötype* is the first portion of the uterus close to the shell gland, where the eggs and yolk cells are formed into eggs proper inclosed in a shell with a lid or *operculum*. In some species the oviduct is provided with a sac-like evagination known as the *receptaculum seminis*, for the storage of the sperm cells. The uterus, which receives the egg, is much convoluted and empties into the genital pore near the cirrus.

The *vitelline glands* are numerous and are situated at each side immediately under the cortical portion of the parasite. Each gland gives off small capillaries that anastomose and unite to form two lateral ducts; these finally unite and constitute the common collecting duct, which empties into the oviduct.

The *shell gland* is relatively large, and consists of numerous glandular cells surrounding the oötype, which receives their secretion.

Function of the Sexual Organs.—The testis generates spermatozoa, which are conveyed through the vas deferens to the cirrus or penis, and are finally discharged into the uterus at the genital pore. From the uterus the spermatozoa travel down the uterus to the oviduct and the receptaculum seminis, when this is present, where they are stored.

The ovary is the seat of the egg cells, which are discharged into the oviduct, where fertilization usually takes place. At this point the fertilized egg receives the reserved food material or yolk from the

vitelline glands, and then passes into the oötype, where it receives the secretion from the shell glands; at this point the shell of the egg and the lid are formed. The matured and fully formed egg now passes to the uterus, and is finally discharged through the genital pore.

The function of Laurer's canal is not well understood; it probably represents a rudimentary vagina, having no external opening, since in Cestoda the receptaculum seminis, when present, is situated near it.

Mode of Fixation.—The trematodes attach themselves to the host by means of their suckers, which are especially well adapted to the purpose through the action of equatorial, meridial, and radial muscular

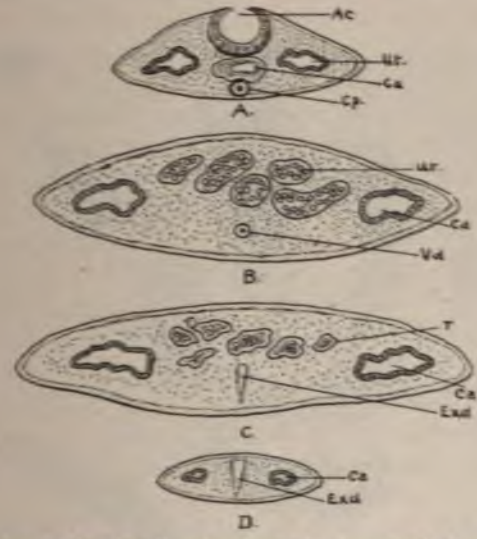


FIG. 100.—Diagram showing the structure of a trematode in sections at different levels. *A*, through the posterior sucker or acetabulum; *B*, posterior to the acetabulum; *C*, about the posterior third; and *D*, at the caudal end. *Ac*, acetabulum; *Ut*, uterus; *Ca*, ceca; *Cp*, cirrus pouch; *Vd*, vas deferens; *T*, testes; *Exd*, excretory duct.

fibers. Certain trematodes appear to wander from place to place, whereas others remain in the same place for a long time producing characteristic local lesions.

Life History.—The life history of endoparasitic trematodes is characterized by an interesting and complicated alternation of generation. The sexual reproduction that takes place in the vertebrate host is followed by two asexual generations in an invertebrate host, in which a complete metamorphosis occurs. Briefly, the life cycle is as follows: On being discharged from the body of the host the egg hatches in water into a ciliated larva termed a *miracidium* (first free larva). This enters into the intermediate host—usually a mollusc—in which it undergoes metamorphosis and gives rise to a *sporocyst*, from which numerous *redia* are produced, each of which may give

rise to a *cercaria* (second free larva). The intermediate host eventually dies and the cercaria are set free. The cercaria attach themselves to grass or weeds at the edges of pools of water, become encysted, and await the coming of the definitive host. On being swallowed by the appropriate animal the cyst is digested, and the free cercaria attaches itself to the mucous membrane of the alimentary canal, or travels to the bile-duct, etc., as the case may be, and there grows into an adult that matures and produces eggs, when the cycle is repeated. The life cycle of the trematodes, therefore, usually requires two hosts. Rare species may require but one host; in such cases the miracidium is able to enter the definitive host and undergo immediate sexual develop-



FIG. 101.—Sporocyst, Rediæ and Cercariæ of Distomum atrovenata of frog.

ment. The full life history of a trematode was first outlined by Thomas in *Fasciola hepatica*, under which heading it will be described in greater detail (Plate VII). Looss has elaborated the life history of *Paramphiostomum cerci*.

Mechanism of Transmission.—Trematodes are usually transmitted in the form of encysted larval *cercaria*. The mode of transmission of the trematodes of the lung (*Paragonimus westermanii*) and of the blood (Schistosoma) was not definitely known until lately, when it was found to be similar to *Fasciola hepatica*. The penetration of the skin by the myracidium as found free in water has been described by Katsurada as occurring in *Schistosoma japonicum*, but has not been definitely proved. Our experiments to bring about infestation of young dogs by the appli-

cation to the skin of the miracidium of *S. japonicum* or by injecting miracidia subcutaneously, were negative.

Habitat.—The trematodes are parasites of all classes of vertebrates, and may lodge in any of the organs; by preference, however, they inhabit the intestine, liver, lungs, and mesenteric vessels.

Pathogenesis.—A small number of trematodes of various species may live in man without giving rise to appreciable symptoms. Large numbers of them and certain species may occasion grave disturbances (Plate III and Fig. 7). The presence of ova circulating in the blood or the occurrence of secondary bacterial infections may lead to serious complications.

Diagnosis.—The existence of trematodes in the intestine and liver can be ascertained by making a careful microscopic examination of the feces, which will result in the finding of eggs or possibly, in rare cases, an adult parasite may be found. In paragonimiasis the eggs of the parasites may be found in the sputum, and in schistosomiasis they can be demonstrated in the urine or in the feces.

Treatment and Prophylaxis.—Since no specific distinctive agent has been found, treatment is, as a rule, unsatisfactory. When the parasites are lodged in the stomach or intestine, chloroform combined with eucalyptol, extract of male-fern, or thymol, employed as described under Ankylostomiasis, may be followed by expulsion of the parasite.

The life history of some trematodes is not sufficiently well known to permit prophylactic measures against the infestation to be employed. As a rule, domestic animals, such as dogs, cats, oxen, horses, and especially sheep, are the indirect sources of infection, and where such animals are known to harbor the parasites, the eating of uncooked green vegetables and of edible snails, should be restricted. The possibility of penetration of the miracidia or other free larvæ of some trematodes through the skin itself suggests the necessity of protecting the feet and hands when working in swampy and moist localities, and of guarding against bathing in contaminated water.

Classification.—The classification of trematodes generally accepted today is that of Burmeister, which was revived by Monticelli in 1892. This classification divides these parasites into the following three orders:

Order I. HETEROCOTYLEA (Monticelli).—Synonyms: Polystoma, Leuckart; Pectobothri, Burmeister; Monogenea, Van Beneden.

As a rule, these are ectoparasites, living on aquatic animals, usually fish; but occasionally they are endoparasites, inhabiting amphibia and tortoises. Since in their ectoparasitic existence they are exposed to external influences, their organs for attachment are well developed and may contain several suckers. Development is direct; they have

only one host, no free larval stage, and undergo no metamorphosis and no alternation of generation.

Order II. ASPIDOCOTYLEA (Monticelli).—Synonyms: Aspidobothri, Burmeister.

These are endoparasitic trematodes of low organization, found in the tortoise, marine fish, and shell-fish. They have one ventral sucker. Development is direct; they have one host and one free larval stage, and undergo no metamorphosis and no alternation of generation.

Order III. MALACOTYLEA (Monticelli).—Synonyms: Distoma, Leuckart; Malacobothri, Burmeister; Digenea, Van Beneden.

These are typical endoparasitic trematodes. They never have more than two suckers and sometimes only one (Monostomidæ). Development is indirect; they have two free larval stages, two hosts, and undergo complete metamorphosis. This order embraces all the parasitic trematodes of man and is subdivided into two groups:

Group A. Metastatica (Leuckart).—Development is indirect, but there is no alteration of generations.

Group B. Digenea (Leuckart).—Development is indirect, with alternation of generations and complete metamorphosis.

The order Digenea embraces all the human parasites and is divided into four families as follows:

Family 1. *Fasciolidæ.*—Digenea with oral and ventral sucker; hermaphroditic, with excretory pore at the posterior end.

Family 2. *Paramphistomidæ.*—Digenea with oral and ventral suckers, the ventral sucker being at the posterior end; hermaphrodites; excretory pore on the dorsal surface.

Family 3. *Monostomidæ.*—Digenea provided with only one oral sucker; ventral sucker absent; hermaphroditic.

Family 4. *Schistosomidæ.*—Digenea resembling Fascio idæ; body elongated; sexes separated.

The following table contains a classification and a brief description of the most important differential characteristics of the parasitic trematodes of man.

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Genus	Species	Size in Millimeters	Habitat
Fasciola.	*F. hepatica.*	20–30×9–13.	Liver.
Fasciolopsis.	*F. buski.*	30–70×14–15.	Intestine.
	F. rathouisi.	20–30×8–12.	Intestine.
Fascioletta	*F. ilocana.*	4–6×0.7–1.0.	Intestine.
Clonorchis.	*C. sinensis.*	12–20×2–4.	Liver.
Opistorchis.	*O. felineus.*	7–12×2–2.5.	Liver.
	O. noverca.	9–12×2.5.	Liver and intestine.
Metorchis.	*M. truncatus.*	2–2.5×0.6.	Liver.
Dicrocelium.	*D. lanceatus.*	5–13×1.5–2.5.	Liver.
Paragonimus.	*P. westermanii.*	8–16×4–8.	Lungs.
Heterophys.	*H. heterphys.*	1–2×0.5–0.7.	Intestine.
Watsonius	*W. watsoni.*	8–10×4–6.	Intestine.
Gastrodiscus.	*G. hominis.*	6–8×3–4.	Intestine.
Monostoma.	*M. lentis.*		Eyes.
Schistosomum	*S. hematobium*	♂ 10–15×1. ♀ 15–20×0.1–0.2.	Portal vein, veins of mesentery, pelvis and bladder.
	S. mansoni.	♂ 12×0.4–0.5. ♀ 14–15×0.1–0.2.	Portal vein, veins of mesentery, pelvis and rectum.
	S. japonicum.	♂ 7–12×0.5. ♀ 8–12×0.4.	Venous and arterial system of liver. Veins of mesentery, pelvis, and rectum.

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CHAPTER XIII

TREMATODA (Continued)

THE PARASITIC TREMATODES OF MAN

Parasitic Trematodes of the Liver.—Parasitic Trematodes of the Intestine.—Parasitic Trematodes of the Lungs.—Parasitic Trematodes of the blood.—Erratic Trematodes.—Laboratory Search and Diagnosis of Trematodes.

For convenience and in order to simplify the clinical study of the parasitic trematodes of man, the system adopted by Brumpt will be followed—that is, the parasites will be divided into four groups, according to their most common habit in the body:

I. Parasitic Trematodes of the Liver.
II. Parasitic Trematodes of the Intestine.
III. Parasitic Trematodes of the Lungs.
IV. Parasitic Trematodes of the Blood.



FIG. 102.—Fasciola hepatica. *A*, showing the general structure, enlarged four times after Sommer and *B*, showing the ramified intestine, after Leuckart. *O*, oral sucker; *D*, digestive tract; *T*, ramified testes; *Vs*, ventral sucker; *Ut*, uterus; *Ov*, ovary; *vg*, vitelline glands. (*In Brumpt.*)

I. PARASITIC TREMATODES OF THE LIVER

The trematodes which are most commonly found in the liver of man are: (1) *Fasciola hepatica;* (2) *F. gigantica;* (3) *Clonorchis sinensis;* (4) *Opisthorchis felineus;* (5) *O. noverca;* (6) *Metorchis truncatum;* (7) *Dicrocelium lanceatum.* Of these, *F. hepatica, D. lanceatum,* etc., are merely occasional parasites of man, whereas *C. sinensis* and *C. felineus* are relatively common.

1. **Fasciola hepatica** (Linnæus, 1758).—*Fasciola hepatica*, the liver "fluke," is a common parasite of sheep, oxen, goats, horses, and other herbivorous animals of Europe, Africa, America, and Asia. The parasite is 2 to 3 cm.

long by 8 to 13 mm. in width. The body is leaf-like in shape, flat and whitish at the center and brown or almost black at the borders, since ramifications of the intestine occur in these regions. The anterior part of the body is well defined into a cephalic cone at the extreme end of which is the oral sucker. The ventral sucker is placed at a point at about the base of the cone, and from 3 to 5 mm. from the oral sucker.

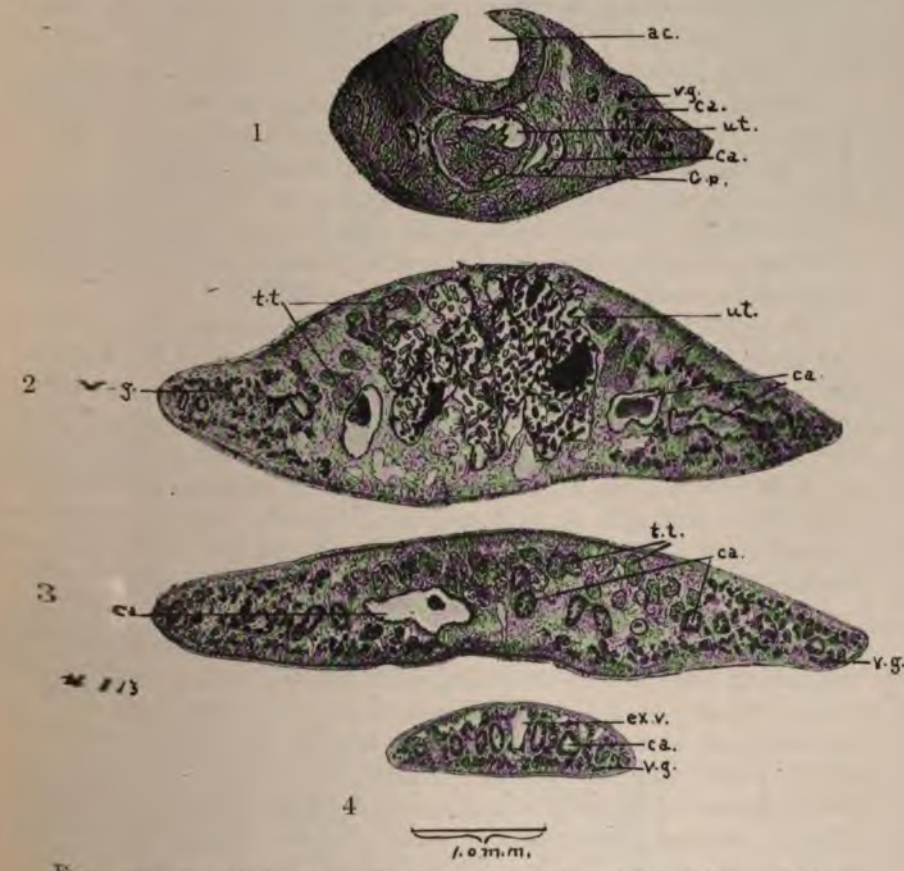


Fig. 103.—Fasciola hepatica. Transverse section through 1, acetabulum; 2, uterus; 3, posterior body third; 4, posterior extremity. *Ac.*, acetabulum; *ca*, cæca; *t.t*, testis; *ut*, uterus with eggs; *v.g.*, vitelline glands; *ex.v*, excretory vesicle; *c.p.*, cirrus pouch.

The digestive tract is freely ramified, and occupies a large part of the body, especially toward the borders, lending a dark color to the parasite at this region.

The male reproductive organs consist of two ramified testes, situated at the middle of the body, one in front of the other, a vas deferens, vesicula seminalis, cirrus, and cirrus pouch. The female organs of

reproduction consist of a single branched ovary, oviduct, and uterus, with its appendages: a vitelline gland, a vitelline duct, and a shell gland. Laurer's canal is also present. The uterus is situated at about the union of the middle with the anterior third of the body, and appears as a coiled structure, bluish black in color, at the middle of the body. The excretory system is well developed. The cuticle is provided with spines. The ventral sucker is near the anterior sucker. The genital pore is in the median line, in front of the ventral sucker.

Diagnosis.—The diagnosis of *Fasciola hepatica* is made by finding the eggs in the feces. The eggs are oval, yellowish brown, thin shelled, operculated, and measure from 130 to 145μ by 70 to 90μ (Fig. 130).

Habitat.—This trematode is commonly found in the bile-ducts of sheep and oxen, and has occasionally been found in man, about twenty cases having been reported. It is also found in buffaloes, goats, horses, pigs, rabbits, and guinea-pigs, and is said to be common in Egypt.

Life History.—*Fasciola hepatica* has a very complicated life history. This embraces an alternation of generation, two free larval stages, two hosts, and a complete metamorphosis (Plate VII).

The egg is fertilized in the oviduct, undergoes cleavage in the uterus, and when it is discharged in the bile-ducts or is found in the feces, it has reached the morula stage. Outside of the host, with sufficient moisture or when deposited in water, and at a temperature of 23° to 26°C., the embryo develops into a ciliated larva, called a *miracidium*, in about two to three weeks. The miracidium measures about 130μ and is provided with an oral sucker, a digestive sac, an excretory system, germ cells, and cilia on the surface of the body. It escapes through the operculum of the egg, becomes free, and swims rapidly in water.

The life duration of the miracidium in the free stage is very short—only about eight hours—but if during this time it is taken up by a young snail, *Limnæa truncatula*, *L. humilis*, *L. viator*, etc., which acts as intermediate host, it enters the lung chambers of the snail, to which it attaches itself and undergoes a metamorphosis. This consists in the disappearance of all larval organs except the germ cells, which develop into a sporoblast and then into a sporocyst, inside of which the further larval stage, named *Redinæ*, after the celebrated biologist Redi, develops. The Redinæ consist of a rudimentary intestine, cuticle, excretory system, rudimentary genital organs, and a genital pore.

The redia now forces its way out of the sporocyst and invades the organs of the snail, especially the liver, where, under favorable conditions of temperature, as during the summer, it develops a caudal appendage and assumes the second larval stage, known as *cercaria*. The latter resembles in many respects a young fasciola with a tail. The cercaria is provided with cuticular glands for the secretion of the cyst-

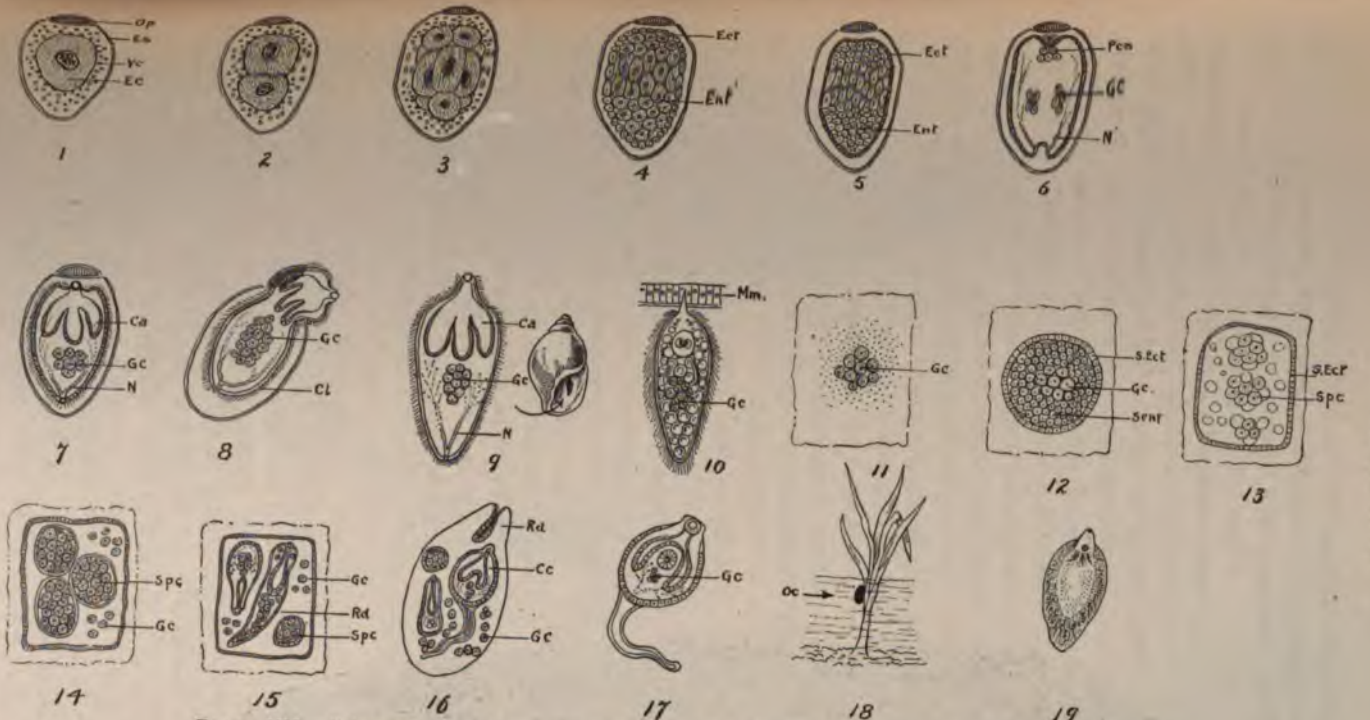


PLATE VII.—Schematic drawing of the life cycle of a digenea trematode (*Fasciola hepatica*).

1, Fertilized egg. *Op*, operculum; *Es*, egg shell; *Yc*, yolk cells; *Ec*, egg cell. 2 and 3, Cleavage states. 4, Cleavage cells differentiating into ectoblast, *Ect*, and entoblast, *Ent*. 5, Ectoblast and entoblast well defined. 6, Development of the miracidium. *Pca*, primitive ceca; *Gc*, germ cells; *N*, nephridium. 7, Fully formed ciliated miracidium enclosed in the egg shell. *Ca*, ceca. 8, Miracidium escaping through the operculum; *Cl*, cilia. 9, Free stage of miracidium, first larval stage, entering the snail. 10, Miracidium penetrating the lung chambers of the snail through the mucous membrane, *Mm*. 11, Metamorphosis and degeneration of all the structures of the miracidium, except the germ cells, *Gc*, in the tissue of the snail. 12, Formation of scondary ectoderm, *Sect*, and secondary entoderm. Sent from the germ cells. 13, Beginning development of sporocyst, *Spc*. 14, Sporocyst stage. 15, Formation of redia, *Rd*, from sporocyst. 16, Formation of cercaria, *Cc*, inside of a redia. 17, Free cercaria, second larval stage. 18, Encysted cercaria attached to a water weed. 19, Adult fasciola, about normal in size.

wall of the next stage. Instead of developing into cercaria the redia may also, under unfavorable conditions of temperature, as during the autumn, give rise by pedogeny to a new brood of sporocysts and rediæ.

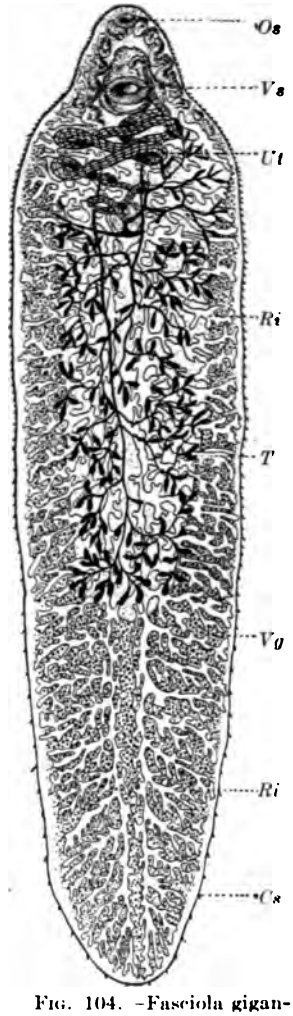


FIG. 104.—Fasciola gigantica. *Os*, oral sucker; *Vs*, ventral sucker; *Ut*, uterus; *Ri*, ramified intestine; *T*, testes; *Vg*, vitellin glands; *Cs*, cuticular spines. (× 4 *after Looss in Brumpt.*)

The infection is usually so great that the snail eventually dies and undergoes disintegration, and the cercaria, being set free, swims in water, attaches itself to a blade of grass or a water weed, loses its tail, becomes encysted, and thus the encysted cercaria stage is effected. On being swallowed by a sheep, the primary host, the cyst is digested and the cecaria, making its way along the bile-duct, lodges in the liver, where in about six weeks it grows into a sexually mature fluke and the cycle is repeated.

Mechanism of Transmission.—Sheep and other susceptible animals are infected by swallowing encysted cercaria.

Pathogenesis.—The liver fluke is the cause of the disease known as "liver rot." It is marked by gastro-intestinal and hepatic disturbances, anemia, more or less pernicious in type, jaundice, etc. The liver shows evidence of the presence of a type of biliary cirrhosis, and the parasite is found lodged in the dilatation of the bile-duct.

2. **Fasciola gigantica** (Cobbold, 1856).—This parasite resembles *Fasciola hepatica*, from which it may be differentiated by its larger size. It measures 2.5 to 7.5 cm. by 3 to 12 mm., and is commonly found in the livers of oxen, goats, giraffes, zebras, etc., in Senegambia. It is believed to have been found but once in the liver of a man.

3. **Clonorchis sinensis** (Cobbold, 1875).—This parasite was discovered by McConnell in 1874 in the liver of a Chinaman. It was at first believed to be Opisthorchis, but in 1907 Looss placed it in the genus Clonorchis. It is one of the most common parasitic trematodes infesting the liver of man, and is especially common in China and Japan, where it has been found in 50 per cent. or more of the cases examined (Katsurada, Leger). It has not as yet been found in the lower animals. Two varieties have been described,

differentiated only by their size. According to some authors (Verdun and Bruyant), both types belong to the same species, whereas according to others (Brown and Looss) each is considered a different species.

Clonorchis sinensis var major (Verdun and Bruyant, 1908).—This parasite is white yellowish, red, or brownish in color. It is narrow, measuring 13 to 19 by 3 to 4 mm. The testes are branched and situated posterior to the ovary; the vitelline glands are placed at each side, between the level of the ventral sucker and the ovary. The genital pore is anterior to the ventral sucker. The eggs are pear-shaped and narrowed toward the anterior end. They have an operculum with sharply projecting brim.



Fig. 105.



Fig. 106.

Fig. 105.—Clonorchis sinensis (from man). *o.s.*, Oral sucker; *ca*, ceca; *vg.*, vitelline glands; *ut*, uterus; *sg*, shell gland; *ov.*, ovary; *t.t.*,[1] anterior testis; *t.t.*,[2] posterior testis.
Fig. 106.—Clonorchis sinensis (from cat).

Clonorchis sinensis var minor (Verdun and Bruyant).—This parasite, also called *C. endemicus* (Baelz, 1883), is almost identical with *C. sinensis var major*, from which it can be differentiated only by its smaller size. It measures from 6 to 13 by 1.8 to 2.6 mm. *C. sinensis var major* has been found only in man, but *C. sinensis var minor* is found in man, cats, hogs, and dogs.

Diagnosis.—The diagnosis of *C. sinensis* can be made only by finding the eggs of the parasite in the feces. These are pear shaped, yellowish brown or dark in color, with distinct operculum, and measure about 29 by 16μ.

Habitat.—*Clonorchis sinensis* is a parasite of the liver, and is found

in the biliary canals of man, dogs, and cats. It is very common in China and Japan.

Life History.—The recent work of Kobayashi has demonstrated the encysted Cercaria of this parasite in the subcutaneous tissue and muscles of several species of fresh water fish which when eaten by a susceptible animal, dogs or cats, the larva is set free within three hours, reaches the bile ducts in fifteen hours and becomes adult in twenty-six days. The first intermediate host is not known but Kabayashi believes it to be a snail probably *Melania libertina.*

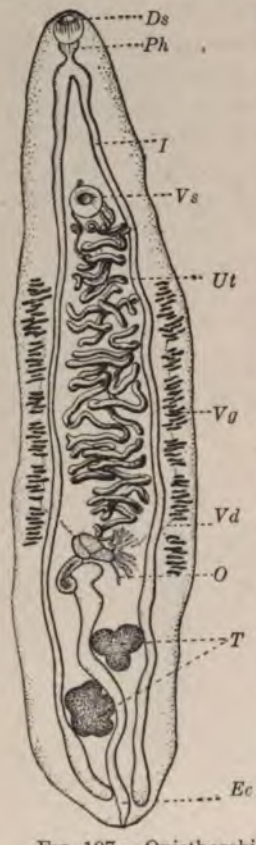


FIG. 107.—Opisthorchis felineus. *Os*, oral sucker; *Ph*, pharynx; *I*, intestine; *Vs*, ventral sucker; *Ut*, uterus; *Vg*, vitelline glands; *Vd*, vitelline duct; *O*, ovary; *I*, testes; *Ec*, excretory canal. (× 12 *after Stiles and Hassal in Brumpt.*)

Pathogenesis.—*Clonorchis sinensis* is the cause of enlargement of the liver and diarrhea.

4. **Opisthorchis felineus** (Rivolta, 1885).—This trematode is lanceolate in shape, the body being long and flat, transparent, and reddish in color. It measures 7 to 12 by 2 to 5 mm. It resembles *Clonorchis sinensis*, from which is differentiated by the testes being lobulated instead of branched. The eggs are oval, operculated, and measure from 26 to 30 by 11 to 15μ.

Habitat.—The parasite is found in the bile-ducts of man, dogs, and cats. It is a common organism, and has been found in various countries of Europe, especially in East Prussia, where Braun found 80 per cent. of the cats to be infected. It is also common in Siberia, and according to Winogradoff, it is more common than are all the other trematodes put together. It is not uncommonly associated with *Dibothriocephalus latus* and *Clonorchis sinensis.*

Diagnosis.—The diagnosis of *O. felineus* is made by finding the eggs in the feces.

Life History.—This is not well known, but Askanazy has demonstrated that infection takes place in man through the eating of fish (*Leuciscus rutilus* and *Idus melanotus*). As these fish frequently feed on a certain mollusk (*Dreyssena polymorpha*), it is probable that the evolution of cercaria takes place in the latter. Prophylaxis against the infection consists in avoiding the eating of improperly cooked fish.

5. **Opisthorchis noverca** (Braun, 1903).—This trematode was found in 1872 by Lewis and Cunningham in the liver of dogs. McConnell

has observed it twice in man in India. The parasite is lanceolate in shape, and in many respects resembles *O. felineus*, except that the anterior part is more rounded and the cuticle is covered with spines. The eggs are operculated, and measure 34 by 21μ. The life history is unknown.

6. Metorchis truncatum (Rudolphi, 1819).—This trematode is somewhat small, measuring 2 to 2.5 by 0.6 mm. The cuticle is provided with spines. The body is slender, with its anterior end pointed and its posterior end truncated. The testes are elliptic. The eggs are operculated, and measure 29 by 11μ. The parasite has been found in seals, deer, and cats. Winogradoff observed the parasite in the liver of a man.

7. Dicrocelium lanceatum (Dendriticum) (Stiles and Hassal, 1897).—This trematode is relatively small. It measures 6 to 12 by 1.5 by 2.5 mm. The body is lanceolate, pointed anteriorly, and so transparent that the coiled and branched uterus is readily visible, filled with eggs, and nearly black in color. The eggs are oval, almost globular, operculated, somewhat flattened on one side, and measure 38 to 45μ by 22 to 30μ. It is characteristic of this parasite that the testes are anterior to the ovaries. The trematode is found in the bile-ducts of sheep, oxen, donkeys, goats, pigs, and rabbits, and it has been observed in man six times.

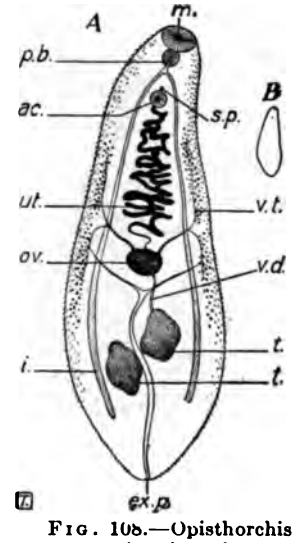


FIG. 108.—Opisthorchis noverca. *A*, enlarged seven times and *B*, natural size. *m*, mouth (oral sucker); *ph*, pharynx; *ac*, acetabulum (ventral sucker); *ut*, uterus; *vt*, vitelline glands; *ov*. ovary; *vd*, vas deferens; *t*, testes; *i*, intestine; *exp*, excretory pore. (*After Manson in Brumpt.*)

II. PARASITIC TREMATODES OF THE INTESTINE

The parasitic trematodes found in the intestine of man are: (1) *Fasciolopsis buski;* (2) *F. rathouisi;* (3) *Fascioletta ilocana;* (4) *Heterophys heterophyis;* (5) *Watsonius watsoni,* and (6) *Gastrodiscus hominis.* These parasites, which up to 1906 were regarded as so rare as to be considered scientific curiosities, have, since then been found to be much more frequent in the intestines of man.

1. **Fasciolopsis buski** (Lankester, 1857).—This parasite is one of the largest trematodes found in man, measuring 3 to 7 cm. by 14 to 15 mm. The body is thick, brownish, and smooth. The oral and ventral suckers are close to each other and near the extreme anterior end of the parasite. The testes are branched, and the genital pore is anterior to the ventral sucker. The eggs are large and oval, yellowish

brown, and resemble the eggs of *F. hepatica*, from which they may be distinguished by the fact that they are slightly smaller in size, measuring 120 to 130 by 70 to 80μ. It is characteristic of this trematode that it has a relatively long cirrus pouch, which extends for about one-fourth the length of the anterior part of the body.

Habitat.—This parasite was first found by Buski in 1843 in the duodenum of a man. It is common in hogs of India and China. According to the observations of Noc and others, it is a somewhat common parasite of man in the Orient.

Diagnosis.—The diagnosis is made from the finding of the eggs or the parasites in the feces, especially after a preliminary treatment by thymol.

Life History.—The life history of *F. buski* is unknown.

Pathogenesis.—In most cases the presence of this trematode in the intestine gives rise to no appreciable symptoms in man,



FIG. 109.—Dicrocelium lanceatum.



FIG. 110.—Fasciolopsis buski.

but it may be the source of gastro-intestinal disturbances associated with dysenteric diarrhea.

2. **Fasciolopsis rathouisi** (Poirier).—Under the name of *F. rathouisi* Poirer described a trematode found in the intestine which resembles *F. buski*, except that it is much smaller. According to d'Odhner, Brumpt, Castellani, and others, this parasite is merely a contracted form of *F. buski*. In 1909 Rodenwaldt described a new species, *Fasciolopsis fülleborni*, found in the feces of an Indian in Hamburg suffering with a fever that was diagnosed as typhoid. According to Brumpt, this parasite is also identical with *F. buski*.

Under the name of "Kwan's fluke," Heanley described a trematode found by Kwan King Hung in a child in Hong-Kong. This parasite was 2 inches in length and ½ inch in breadth, and resembled *F. buski*, except that spines were present on the cuticle.

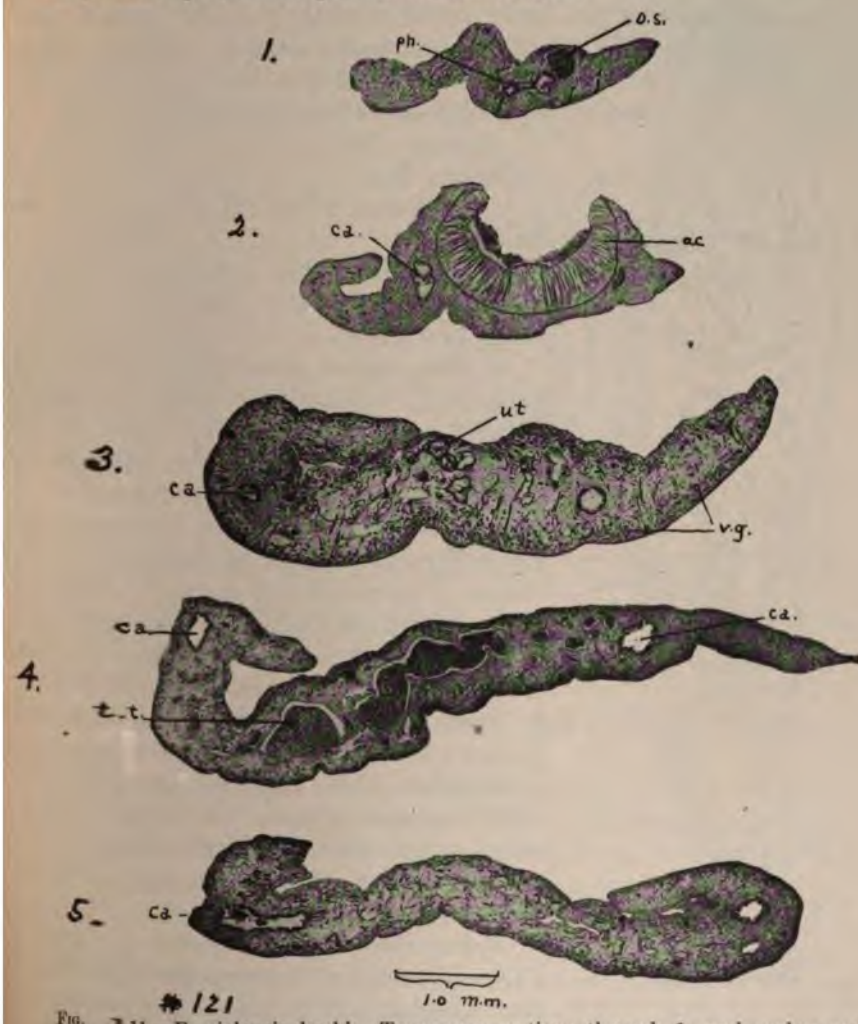


FIG. 111.—Fasciolopsis buski. Transverse sections through 1, oral sucker and pharynx close to cæcal bifurcation; 2, acetabulum; 3, uterus; 4, testes; 5, posterior body extremity.

ac., acetabulum; *ca.*, cæca; *t.t.*, testis; *ut.*, uterus; *v.g.*, vitelline glands; *o.s.*, oral sucker. Left margin of parasite bent ventrally.

3. **Fascioletta (Echinostoma) ilocanum** (Garrison, 1908).—This parasite was discovered by Garrison in 1907 in the feces of a Philippine prisoner. It is small, transparent, reddish in color, and measures 4 to 6 mm. in length by 0.75 to 1.35 mm. in breadth and 0.5 to 1 mm. in

thickness. The body is narrow and attenuated posteriorly. The ventral sucker is almost three times as large as the oral sucker; the genital pore is situated anterior to the ventral sucker; the cirrus pouch is well developed, and the vesiculæ seminalis is situated posteriorly to it. The testes are bilobed and posterior to the ovaries. The eggs are operculated, measuring 100μ by 55 to 65μ, and contain miracidia.

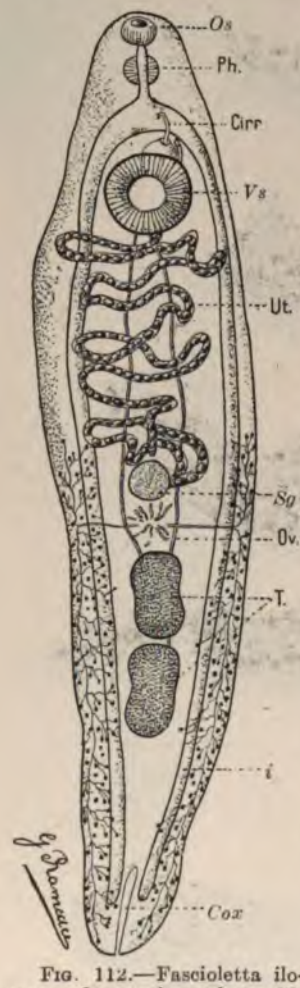


FIG. 112.—Fascioletta ilocana. *Os*, oral sucker; *Ph*, pharynx; *Cirre*, cirrus; *Vs*, ventral sucker; *Ut*, uterus; *Sg*, shell gland; *T*, testes; *i*, intestine; *Ec*, excretory canal. (× 25 *partially after Garrison in Brumpt.*)

Habitat.—The parasite inhabits the intestines of man.

Life History.—The life history is unknown.

Pathogenesis.—The parasite does not appear to produce any appreciable disturbance in the host.

4. **Heterophyes heterophyes** (von Siebold, 1852).—This trematode was found by Bilharz in Egypt in 1851. It is the smallest parasitic trematode of man, being only 1 to 2 mm. in length and 0.5 to 0.7 mm. in breadth. The body is attenuated anteriorly and broad posteriorly. The cuticle is provided with spines in the anterior half of the body. The genital pore is situated posterior to the ventral sucker. The eggs are small, operculated, brownish in color, somewhat thick shelled, and measure 20 to 30μ by 16μ.

Habitat.—This parasite inhabits the small intestine of man. It has also been found in cats, dogs, and birds in Egypt.

Life History.—The life history is not known.

Pathogenesis.—This parasite is probably the source of gastro-intestinal irritation, since it has been found in cases of diarrhea and dysentery accompanied by hematuria.

5. **Watsonius watsoni** (Stiles and Goldberger, 1910).—This trematode was found by Watson in Africa in a case of diarrhea. The body is pear shaped, slightly globular, and reddish in color. It measures 8 to 10 mm. in length by 4 to 5 mm. in width, and about 4 mm. in thickness. The oral sucker is small and often invaginated; the ventral sucker is large

and subterminal; the genital pore is situated posterior to the oral sucker, and at the level of the bifurcation of the intestine. The testes are deeply lobulated, and are situated anteriorly to the ovary; the vas deferens runs into the vesiculæ seminales before opening into the cirrus canal. The eggs are large, measuring 130μ in length by 75 to 80μ in width.

Habitat.—This trematode has been found in the upper part of the small intestine of man,



FIG. 113.

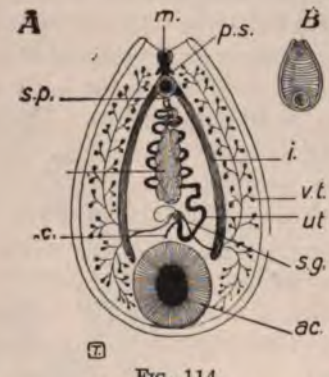


FIG. 114.

FIG. 113.—Heterophyes heterophyes. *a*, Schematic × 35; *b*, natural size; *c*, eggs × 250; *d*, spine × 700. (*After Looss, from Braun's Animal Parasites of Man, English edition.*)

FIG. 114.—Cladorchis (Watsonius) watsoni. A, enlarged four times; *B*, natural size. *M*, mouth and oral sucker; *ps*, esophagus (?); *Sp.*, genital pore; *i*, intestine; *t*, testes; *vt*, vitellin glands; *sg*, shell gland; C, Laurel canal (?); *ac.*, acetabulum. (*After Shipley in Brumpt.*)

especially in children, but it is believed that its host is usually a herbivorous animal.

Life History.—The life history of this parasite is not known. Looss suggested that the evolution is similar to that of *F. hepatica*, and that the intermediate host is a mollusk (*Physa alexandrina, P. micropleura*).

Pathogenesis.—The parasite may cause congestion of the mucosa of the intestine, diarrhea, and anemia.



FIG. 115.—Gastrodiscus hominis. (*Natural size after Manson in Brumpt.*)

6. **Gastrodiscus hominis** (Lewis and McConnell, 1876).—This parasite is a flask-shaped trematode, reddish in color, found in the cecum and ascending colon of man. It is from 6 to 8 mm. in length, 3 to 4 mm. in width, and 2 mm. in thickness. The body is divided into an elongated conical anterior portion and an enlarged, dish-shaped posterior end. The small oral sucker is located somewhat ventrally and the large posterior sucker is at the border of the posterior disc. The genital pore is situated anteriorly to the disc, and at about the middle of the anterior portion. The testes are

lobulated. The eggs are operculated, and about 150μ in length by 72μ in width.

Habitat.—The parasite was found by O'Brien and Curran in the cecum and ascending colon of a man in India.

Life History.—The life history is not known.

7. **Metagonimus yokogawai** (Katsurada, 1913).—This trematode, which is found in man and mammals in Japan, resembles *Heterophyes heterophyes* with which it is probably identical. Katsurada, however, believes it to be a new species. The body is elliptic in shape, and from 1 to 1.5 mm. in length by 0.4 to 0.9 mm. in width. The cuticle is covered with spines. The ventral sucker is characteristic in that it is a sac-like structure placed deep within the body and not protruding on the ventral surface, as in other flukes. The testes are elliptic and situated at the posterior end of the body. Vesicula seminalis, cirrus pouch, receptaculum seminis, and Laurer's canal are all present. The eggs are elliptic, yellowish brown in color, and measure 28 by 16μ. They resemble the eggs of *Clonorchis sinensis*, from which they may be differentiated by the absence of shoulders below the operculum. The genital opening is in front of the ventral sucker.

Habitat.—This trematode is found chiefly in the jejunum, and rarely in the cecum.

Life History.—The cercarial stage occurs in the trout, *Plecoglossus altivalis* and infection takes place through the eating of this improperly cooked fish.

Pathogenesis.—The parasite is the cause of a chronic catarrhal enteritis. The organism penetrates deeply into the mucosa, but not into the submucosa, and may invade and destroy the solitary glands.

III. PARASITIC TREMATODES OF THE LUNGS

Some of the parasites of the liver have occasionally been found in the lungs, but only one species, *Paragonimus westermanni*, appears to inhabit this organ.

Paragonimus westermanii (ringeri)—(Kerbert, 1878). *History.* This worm was discovered by Kerbert in the lungs of tigers in 1878, and in 1880 Baelz found its eggs in the sputum in cases of hemoptysis. Later Ringer, and in 1893 Baelz, found the parasite in the lungs of man. In 1890 Otani and Yamagiwa found it in the brain in a case of Jacksonian epilepsy, and Stiles and Looss defined the zoölogic position of the parasite. It has also been found in cats (Ward, Weidman), in dogs (Railliet), and in hogs (Stiles). The best description of the lesions caused by this parasite is that of Musgrave, who in 1907 found it in the Philippine Islands. The parasite is common in Japan, China, Korea, and North America. Naunyn found it in man in Mexico.

Morphology.—The body of the adult parasite is reddish brown or slate colored, and on exposure to the air it becomes brown and grayish. Specimens preserved in alcohol, formaldehyd, etc., bear a striking resemblance to a raw coffee-grain, both in size and color. It is oval in shape and thick, with a slightly flattened ventral surface. It measures 8 to 16 mm. in length, 4 to 8 mm. in width, and 3 to 4 mm. in thickness. The cuticle is covered with spines. On the ventral surface both suckers are visible to the naked eye and of about equal size. The oral sucker is at the anterior end, somewhat ventrally situated, and the ventral sucker is slightly anterior to the middle of the body on the midline. The genital pore is situated behind the posterior



FIG. 116.—Paragonimus westermanii. *a*, Schematic × 8; *b*, eggs × 300; *c*, natural size. (*After Looss in Castellani and Chalmers.*)

sucker. The testes are usually ramified, and are placed at each side, behind the ovary and uterus. The eggs are oval, operculated, somewhat barrel shaped, light yellow or reddish brown in color, and from 80 to 100μ in length by 50 to 75μ in width. The excretory vesicle is well developed (Fig. 116).

Habitat.—This is a parasite of the lung, and has been found in man, tigers, cats (Plate III) dogs, and especially in hogs in Asia and North America. It may be found as an erratic parasite in other organs such as the brain and the liver.

Diagnosis.—The diagnosis is made by finding the eggs in the sputum.

Life History.—The life history of Paragonimus westermanii, according to Nakagawa, requires two intermediate hosts: a mollusk

Melania libertina, m. tuberculata, etc., in which the miracidium undergoes the first development and a crustacean *Pantamon obtusipes* in which it becomes encysted. Iturbe in Caracas, in his work on this important question has shown that in Venezuela, the primary intermediate host is the snail *Ampullaria luteostoma* and that the encystment of the cercaria takes place in the crab *Pseudothelphusa iturbei*, which probably is the transmitter of the parasite to man and animals.

Pathogenesis.—This trematode is the cause of a chronic affection of the lung that clinically resembles chronic fibroid phthisis (Plate III and Fig. 7). The disease is known as "Oriental hemoptysis," "parasitic hemoptysis," or paragonomiasis.



FIG. 117.—Paragonimus westermanii not full grown.



FIG. 118.—Ovum of Paragonimus westermanii, showing the operculum, *op*, at one pole and the miracidium; *mc*, within the egg shell.

IV. PARASITIC TREMATODES OF THE BLOOD

Three species of trematodes, all belonging to the family Schistosomidæ, have been found in the blood of man; namely, *Schistosomum hematobium, S. mansoni,* and *S. japonicum.*

1. **Schistosomum hematobium** (Bilharz, 1852). *History.*—*Schistosomum hematobium* was found by Bilharz in 1852 in the portal vein of man in Egypt, and in 1864 it was found by Harley in a patient from the cape of Good Hope. Since then it has been found widely distributed throughout Africa, Asia, Persia, and India. Other species have been discovered in sheep, horses, oxen, monkeys, etc.

The parasite is remarkable in that, unlike all other trematodes, it is bisexual.

Male.—The male is long, apparently round and slender, resembling a nematode. It is whitish in color, and measures 12 to 14 mm.

in length and about 1 mm. in width, but it is really flat and thin. The body is provided with two lateral flaps or wings, commonly turned inward and ventrally, inclosing a canal, known as the "*gynecophoric canal*," for the reception of the female. This gives the worm its apparent cylindric form. The cuticle is provided with short spines, by means of which the parasite is probably capable of clinging to the walls of the blood-vessels. The oral sucker looks ventrally, and the central sucker is near the anterior part of the body. The genital pore is posterior to the ventral sucker.

The digestive tract consists of a mouth and a long esophagus, provided with numerous glands and intestine. There is no pharynx. The esophagus bifurcates at the level of the ventral sucker, and is continued by the intestinal ceca, which, after anastomosing at some points, finally unites behind the testes into a common trunk. The excretory pore is at the posterior end and situated somewhat dorsally.

The reproductive organs consist of a chain of oval or round testes, four or five in number, a vas deferens which runs into the vesicula seminalis, is continued by the ejaculatory duct, and opens into the genital pore behind the ventral sucker.

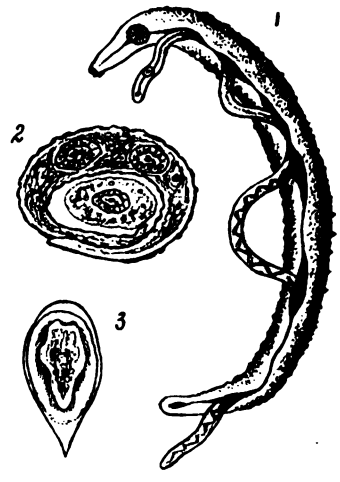


FIG. 119.—Schistosomum hematobium. 1, Male and female; female worm enclosed in the gynecophoric canal of the male (modified after Looss); 2, transverse section; 3, egg.

Female.—The female is elongated and slender and the body is so rolled up as to make it appear filiform and cylindrical in shape. It is about 15 to 20 mm. in length, about 100μ anteriorly, and 250μ posteriorly in width. Like the male, it has an oral and a ventral sucker. The alimentary canal is similar to that in the male, and its contents give the parasite its characteristic dark-brown color. The cuticle is smooth, except at the sucker and at the posterior end, where it is provided with a few spines. The reproductive organs consist of a single ovary, an ovarian duct, and the uterus. In its course the duct receives the vitelline duct from a single yolk gland. The genital pore is situated behind the ventral sucker. The uterus contains only a few eggs, which, when discharged, measure 120 to 190μ in length and 50 to 75μ in width. They are not operculated, are relatively thick shelled, and are provided with a terminal spine. Each contains a miracidium (Fig. 120).

Habitat.—The parasite inhabits the portal venous system of man, and has once been found in a monkey (Cobbold). The two sexes may

be found together or separated in the portal vein and its branches and in the mesenteric and splenic vein, and also in the small veins of the pelvis (vesical, uterine, and hemorrhoidal). It is rarely found in the vena cava or in the lung. The number of parasites found varies from two to several hundred. The females may migrate to the small veins and venules of the bladder, where they have been found lodged in the submucosa.

Life History.—According to Looss, the adult female, lodged in the veins of the bladder, can push her head (close to which is the genital pore) into the capillaries, and when the eggs are discharged, they may gradually work their way, as foreign bodies, into the capillaries of the submucosa, and by ulceration of this membrane into the bladder, be discharged with the urine. The eggs discharged by the female measure 80 to 90μ in length by 30 to 40μ in breadth. During its journey through the walls of the bladder, however, the egg undergoes development and increases in size, so that when voided with the urine it measures 130 to 190μ in length by 50 to 75μ in breadth, and contains a well-developed miracidium.



FIG. 120.—Ovum of Schistosomum hematobium.

Unless the egg gains access to water soon after leaving the bladder, it will die, but under favorable conditions, it will hatch a miracidium which swims actively. What became of the miracidium was not known until recently Leiper found that the embryos were attracted by several species of snails, particularly by the species *Bullinus contortus* in the body of which they undergo development into sporocysts, radia and cercaria which finally are discharged in the water.

Mechanism of Transmission.—Infection may take place by drinking water containing cercaria or by bathing in it since the cercaria, according to Leiper are capable of penetrating through the mucous membrane or skin.

Diagnosis.—The diagnosis of *Schistosomum hematobium* is based chiefly upon the finding of the eggs of the parasites in the urine. If possible, the urine should be examined during an attack of hematuria, when the eggs are generally more abundant. This urine is centrifugalized, and the sediment examined under the microscope. The eggs are easily recognized by their size and shape. They are oval, relatively thin shelled, and from 130 to 150μ in length by 40 to 60μ in breadth. They are provided with a terminal spine, and contain a ciliated larva (miracidium) which not uncommonly, under favorable conditions, is seen to move, more especially if the sediment is pre-

iously diluted with a little water. It should be remembered that ıe eggs may also, although rarely, be found in the feces and sputum.

Pathogenesis.—Schistosomum hematobium is the cause of urinary histosomiasis, a disease that is characterized chiefly by periodic tacks of hematuria and cystitis (Fig. 121).

2. **Schistosomum Mansoni** (Sambon, 1907). *History.*—It was ıerally known for some time, that two kinds of eggs are present ı cases of schistosomiasis. Manson, in 1903, noticed in the West ıdies that cases of schistosomiasis affecting the rectum and not

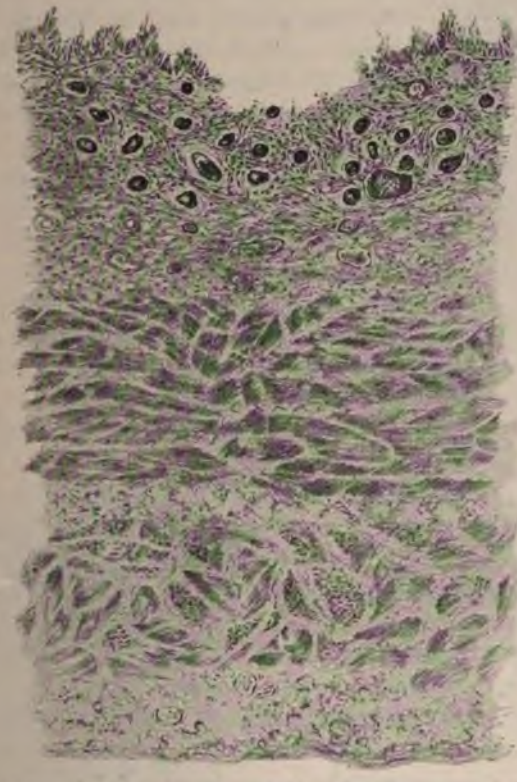


Fig. 121.—Eggs of Schistosoma hematobium in the mucosa of the bladder.

the bladder, the eggs found in the feces were provided with lateral spines. He suggested, therefore, the existence of a separate species of Schistosomum. In an autopsy made in Bahia (Brazil) Piraja da Silva found 24 parasites in the portal vein (19 males isolated, 2 paired and one single). Contrary to *Schistosomum hematobium*, these parasites were not present in the walls of the bladder. Sambon in 1907 created a species, *Schistosoma mansoni*, for these trematodes.

For all practical purposes, the morphology and structure of *S.*

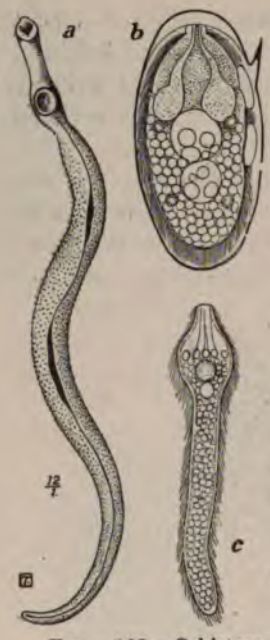


FIG. 122.—Schistosomum mansoni. *a*, Male; *b*, egg; *c*, larva. (*After Holcomb in Castellani and Chalmers.*)

mansoni are similar to those of *S. hematobium*, except for the presence of a lateral spine in the egg, which can be seen even in the uterus, due to the difference in the genital tract described by Fritch. The egg is about 150μ in length by about 60μ in width (Figs. 122 and 123). Other minor differences are described below, under the head of *Schistosomum japonicum*.

Habitat.—The adult worm has been found only in the venous system of man, especially in the portal vein and its branches, but more rarely, also, in the veins of the rectum. The eggs are found in the liver and walls of the rectum and in the feces, but not in the bladder nor in the urine.

Life History.—The eggs are found in abundance in the feces, and under favorable conditions of moisture and temperature the miracidia escape, but nothing definite was known of the further development of the parasite. Its frequent occurrence in association with ankylostoma had suggested that both may have a similar mode of transmission.

Iturbe, in his recent work on the life history of *Schistosoma mansoni*, has succeeded in infecting snails with the miracidium of the parasite. According to this author the intermediate host of *S. mansoni* is a sweet water snail. *Planorbis gudelupensis*, commonly found in Caracas (Venezuela). Iturbe observed the development of sporocysts, radia and cercaria in the body of the snail and describes as characteristic the bifurcated shape of the tail of this cercaria. He likewise proved that infection of the laboratory animals (white mice) readily took place by feeding these animals with the liver of the snails containing the cercaria.



FIG. 123.—Ovum of Schistosomum mansoni from feces.

Pathogenesis.—*Schistosomum mansoni* is the cause of intestinal schistosomiasis.

3. **Schistosomum japonicum** (Katsurada, 1904). *History.*—In 1887 Majima called attention to a peculiar disease seen in Japan, characterized by painful enlargement of the spleen or liver, fever, diarrhea with mucus and blood in the stools, weakness, and emaciation. The designation "Katayama disease" was given to the condition, being named for a town in Bingo in which it was common. Majima attributed the disease to the eggs of some unknown parasite which he found in the liver. His discovery was confirmed by the finding of ova in other organs. In 1904 Katsurada found the adult parasite in cats, and named it *Schistosomum japonicum.* In the same year Fujinami and in 1905 Catto found the parasite in man, and Stiles and Looss gave an account of the disease.

Although *Schistosomum hematobium* and *Schistosomum mansoni* are almost identical morphologically, *Schistosomum japonicum* is easily differentiated by its much smaller size. The adult male is from 7 to 12 mm. in length by 0.5 mm. in breadth, and the adult female is from 8 to 12 mm. in length by 0.4 mm. in breadth. The ventral sucker is relatively larger than the oral. The eggs have no spines, are smaller in size, measuring 60 to 90μ in length by 30 to 50μ in breadth, are oval or globular in shape, and have thick shells and no operculum. Catto points out that the eggs may be mistaken for those of *Ankylostoma duodenalis*, but they really bear a stronger resemblance to the eggs of ascaris, in so far as they are provided with a relatively thick shell.

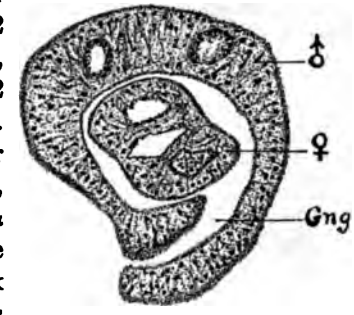


FIG. 124.—Schistosoma japonicum; the male, ♂, containing the female, ♀, in the gyneacophorous groove, *Gng*.

Habitat.—The adult parasite lives in the veins and arteries of the liver and in the mesenteric and pelvic veins of man (Katsurada, Fujinami, Catto). It has also been found in Japan, in cats, dogs, horses, and cattle. The eggs may be found in the liver, but are most often seen in the lymph-nodes of the pelvis and in the submucosa of the rectum.

Life History.—The eggs are discharged with the feces. They contain a miracidium and under favorable temperature conditions, and especially if the feces are diluted with water, the larva (miracidium) hatches in from twelve to eighteen hours, becomes free, and swims freely about. Occasionally the miracidia escape in a short time, or may even be found free in the feces and be mistaken for infusoria. The escape of the miracidium is effected by rupture of the shell of the egg, which swells in water. The shell gradually becomes thinner until it

appears as a delicate line under the microscope. When the miracidium is about to hatch the diameter of the egg is about twice as large as, and the thickness of the shell about one-fourth the size of, the original. At this stage the larva is seen to move freely in all directions, striking the thinned wall from time to time until it finally ruptures (Fig. 125). What became of the miracidium was not definitely known until the recent mark of Miyairi and Suzuki, in Japan, who found that the intermediate host of the parasite is a snail, *Katayama* (*Blaufordia*) *nosophora* in which the miracidium undergoes development into radia and cercaria.

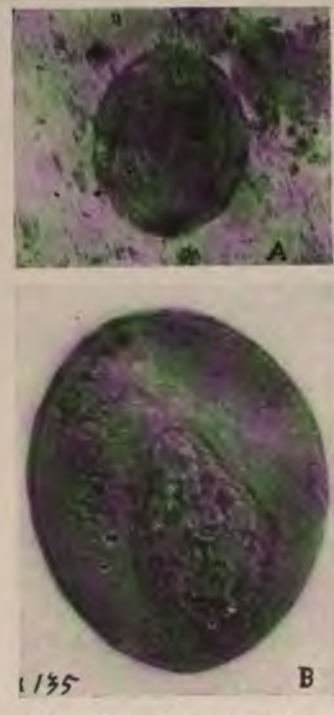


FIG. 125.—Ova of Schistosomum japonicum. *A*, as passed in feces; *B*, swollen and with ciliated miracidium after immersion for some (less than 17) hours in water.

Mechanism of Transmission.—Katsurada and Hashegawa claimed that if a dog was immersed for one hour in water polluted with the miracidium of *Schistosomum japonicum*, the animal becomes heavily infested with the parasite. In their experiments, these authors used a device by means of which the animal could swim without swallowing the water, and as a result came to the conclusion that infestation took place through the skin. The possibility of infection occurring through the mouth, as the result of the animal licking its body after the operation and swallowing an encysted larva (not yet discovered), which could have become attached to the surface during exposure in the water, suggests itself.

Katsurada and Hashegawa were of the opinion that the miracidium represented the infective stage in the life history of the parasite, and that infestation took place through the skin. In this connection it may be said that the result of the writer's experiments were negative. Fresh cultures of the ova of *S. japonicum*, containing numerous free miracidia, were applied to the thin skin of the inguinal region of a young male dog by putting the culture in a test-tube, and applying the mouth of the tube to the skin, the tube being inverted and held in position so that the culture was brought in direct contact with the skin. Two applications were made—one for one hour and the other for one and one-half hours at two different places, a bit of skin being removed from one of them for section after the experiment. The

material was also applied to the prepuce, and, further, 2 c.c. of the culture, containing about 400 free miracidia, were injected subcuta-



FIG. 126.—Schistosomum japonicum in thrombus from mesenteric veins. Transverse sections of three pairs at different levels. *a*, Male, enclosing female; *b*, in gynecophoric canal; *c*, clot from vein.

neously into the same dog. The number of miracidia present was determined by making a stained preparation of a given quantity of the culture and counting them under the microscope by the aid of the mechanical stage. Repeated examinations of the feces for the eggs of schistosoma were negative; sections of the skin failed to show any penetration of the miracidia, and finally, in the autopsy made on the dog after three months, the parasite was not found.



FIG. 127.—Section of the liver from a case of Schistosomiasis (S. japonicum) showing the eggs of the parasite at *A*, lodged in the interlobular spaces.

We were of the belief at the time that the transmission of *Schistosoma japonicum* was through the mouth or through the skin, but by a more developed form of larva than the miracidium. This view has been confirmed by the later work of Miyairi and Suzuki and Leiper and Atkinson who showed that a snail, *Katayama* (*Blanfordia*) *nosophora*, is the intermediate host of the parasite, and that infection takes place through the mouth or by penetration of the cercaria through the skin.



FIG. 128.—Section of a pelvic lymph node from a case of Schistosomiasis (*Schistoso iaponicum*) showing the ova of the parasite, *ov*, in the lymph follicles.



FIG. 129.—Ova of Schistosoma japonicum in the mucosa of the rectum.

Pathogenesis.—The presence of *Schistosomum japonicum* in man, and the accumulation of its eggs in the walls of the rectum, liver, and other organs, give rise to a special disease called "dysenteric schistosomiasis, arteriovenosa, or "Katayama disease (Fig. 129)."

DIFFERENTIAL CHARACTERISTICS OF SCHISTOSOMUM HEMATOBIUM, S. MANSONI, AND S. JAPONICUM

	Schistosomum hematobium	Schistosomum mansoni	Schistosomum japonicum
Size	Male, 12–14 mm. in length by 1 mm. in width. Female, 15–70 mm. in length by 1–0.2 mm. in width.	Male about 12 mm. in length by about 0.4–0.5 mm. in width. Female, 14.5–15 mm. in length by 0.1–0.2 mm. in width.	Male, small, 7–12 mm. in length by about 0.5 mm. in width. Female, 8–12 mm. in length by 0.4 mm. in width.
Suckers	Oral and ventral sucker about the same size.	Oral and ventral suckers about the same size.	Ventral sucker larger than oral.
Habitat	Adult parasite is found in the portal vein and its branches, mesenteric and splenic, and in the vena cava; veins of the bladder and rectum.	Adult parasite is found in the vena porta and its branches; veins of the rectum, but not of the bladder.	Adult parasite found in the venous and arterial systems of the liver, mesentery, and pelvis, especially the rectum.
Eggs	Oval, and provided with terminal spines. They measure 120–190μ in length by 50–75μ in width. Shell relatively thick, chiefly found in the urine and occasionally in the feces	Oval, and provided with lateral spines. They measure about 150μ in length by 60μ in width, with about 18μ as the length of the speculum. Found in the feces but not in the urine.	Oval or almost globular and without spines. Smaller than the other two. Measure 60–90μ in length by 30–50μ in width; shell relatively thick; found chiefly in the feces; occasionally in the urine.
Chief symptoms	Periodic hematuria, occasional diarrhea, but not dysentery. Anemia, cachexia, weakness, and emaciation.	Periodic dysenteric attacks, hematuria usually absent. Anemia, emaciation, and weakness.	Periodic dysenteric attacks, cirrhosis of the liver; swelling of the spleen; anemia, cachexia, and general weakness.

V. ERRATIC TREMATODES

Erratic trematodes are those parasites found occasionally in organs or tissues not usually inhabited by them. Among the most important trematodes that have been found in man in abnormal localities four species may be mentioned; namely: *Fasciola hepatica*, *F. gigantica*, *Schistosomum hematobium*, and *Paragonimus westermanii*.

Fasciola hepatica.—This fluke has been found in the blood-vessels and in the lungs. From our knowledge of the life history of *Fasciola hepatica*, it is hard to understand how it can reach the circulation. On being set free the encysted cercaria in the stomach and small intestine is believed to reach the liver by way of the gall-bladder and become lodged in the bile-ducts, but it is possible that, by perforating the duct and falling into the branches of the hepatic vein, it may reach the vena cava, be carried to the heart, and so become lodged in the

lungs. Furthermore, since the cercaria which measures about 230μ is capable of undergoing elongation, it may become so thinned as to pass the pulmonary circulation and, on reaching the left side of the heart, may be carried by the blood-stream to other organs or tissues. It may even be admitted that such mechanism is common, but as the chemistry of organs other than the liver is usually unfavorable to the growth of the parasite, most of the cercaria perish elsewhere than in the liver, and the cases on record merely represent the few instances of survival.

Fasciola hepatica has also been found in the portal vein and its branches, in the anterior tibial vein, and in the subcutaneous tissues. It is probable also that the parasite found by Nordman in 1832 in the crystalline lens and described under the name of *Monostomum lentis*, and that *Distoma oculi humani* (Ammon, 1833) and *Distoma ophthalmobium* (Diesing, 1850) are merely aberrant young or imperfectly developed types of *Fasciola hepatica*.

Fasciola gigantica.—This was found by Gouvea in the lungs.

Paragonimus westermanii.—This trematode, which usually inhabits the lungs, was found by Otani and Yamagiwa in the brain. It has also been known to occur in the liver. The explanation given for the abnormal location of *Fasciola hepatica* may also be applied to *P. westermanii*. The life cycle of the parasite being similar to *F. hepatica*, the cercaria on being set free in the stomach and intestine, may reach the liver by way of the gall-bladder, or enter the circulation by piercing the bile-duct, or it may gain entrance into the peritoneum by piercing the walls of the intestine. On reaching the right side of the heart it is carried to the lungs, where it finds an appropriate setting for growth and development. It is possible, however, that, as with *F. hepatica*, an occasional cercaria may pass the pulmonary circulation and, on reaching the left heart, be carried to other parts of the body.

Schistosomum hematobium.—The eggs of this parasite have been often found in various parts of the body, and the adult worm has been seen in the veins of the lung. Since it is known that this trematode inhabits the veins of the pelvis and the vena cava, it may readily be understood how it may be carried to the right side of the heart and become lodged in the lungs.

Laboratory Diagnosis of Trematodes.—The study of certain species as, for example, *Fasciola hepatica*, may be followed through all the stages of development from the egg to the adult parasite, but nevertheless, in spite of the numerous researches made, the life history of most trematodes was until recently but imperfectly understood. The study and identification of these parasites, therefore, include the search

for the eggs, the larval forms, and the adult parasite, in man or animals, as the case may be.

Search for the Eggs.—The eggs of trematodes may be found in the feces, in the urine, in the sputum, or in the tissue and organs of the host, as the case may be. In the majority of instances a fresh cover-glass preparation of the material, previously softened, if necessary, in a little water, is sufficient, or the feces may be dissolved in an excess of water, centrifugalized, and the sediment examined. If possible, the suspected material should be collected from the second stool following a mild purge, and in cases of schistosomiasis the material should be gathered during a dysenteric attack.

In order to detect the eggs in the urine, this should be centrifugalized and the sediment examined. If possible, the specimen for examination should be collected during an attack of hematuria.

To find the eggs in the sputum, in cases of paragonimiasis, direct examination of a fresh cover-glass preparation may suffice, or the sputum may be digested in a few cubic centimeters of a 10 to 30 per cent. solution of caustic soda, after which the mixture should be diluted with water, centrifugalized, and the sediment examined. If possible, the material for examination should be collected during an attack of hemoptysis.

Eggs in tissues and organs are found by microscopic examination of the section, or, as preferred by some, the material may be finely teased and digested in a few cubic centimeters of 10 to 30 per cent. caustic soda solution, diluted with water, centrifugalized, and the sediment examined. In the liver, the eggs of *Fasciola hepatica* are found in the perilobular spaces, along the course and in the lumen of the bile-ducts, and the eggs of Schistosomum are seen in the lumen and in the branches of the portal vein. Sometimes the eggs may be lodged in the capillaries of the lobules or in the central lobular vein.

One of the characteristics by which a trematode egg can be recognized is by the presence of an operculum at one of the poles—except in the case of Schistosomum eggs, which are not operculated. Trematode eggs, as a rule, have a thin shell, with the exception of Schistosomum, whose egg in this respect resembles that of an ascaris. The eggs of *S. hematobium* are provided with terminal spines and those of *S. mansoni* with lateral spines. Other trematode eggs have no spines. The eggs of most trematodes, when found in the feces, contain a ciliated larva (miracidium); this is not true of *Fasciola hepatica*, *Fascioletta ilocanum*, and a few other species of less importance. The egg of *Schistosomum hematobium*, as found in the urine, usually does not contain a miracidium, but will develop one if water be added to the urine, which is then permitted to stand over night. In the accom-

panying table the differential points of importance for recognizing the eggs of trematodes are given.

Search for Trematodes in the Larval Stage.—The larvæ of trematodes parasitic in the lower animals are relatively easy to find by making a systematic study of a certain number of aquatic mollusks (Planorbes, Limnæ, Physa, etc.) found on the banks of rivers and creeks, or in stagnant water frequented by frogs, fishes, and birds. The larval stages—sporocysts, rediæ and cercaria—are found abundantly in the internal organs, especially the lungs and liver. The liver of a snail (gastropod) is usually located near the pointed end of the shell. It is sufficient, therefore to cut through this part, remove the liver—which may be recognized by its dark-brown color—moisten it with a

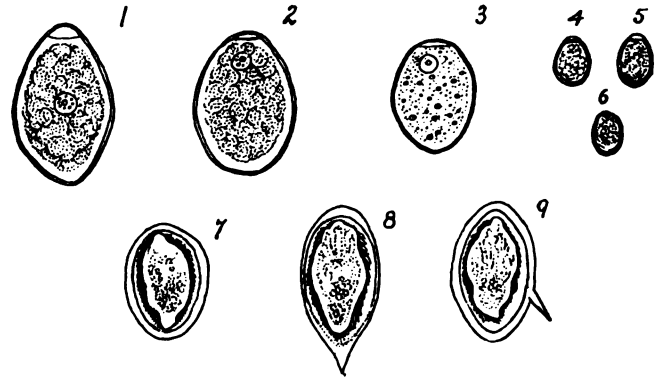


FIG. 130.—Eggs of trematodes. 1, Fasciolopsis buski; 2, Fasciola hepatica; 3, Paragonimus; 4, Opisthorchis noverca; 5, Clonorchis sinensis; 6, Heterophyes heterophyes; 7, Schistosomum japonicum; 8, Schistosomum hematobium; 9, Schistosomum mansoni.

little salt solution, tease the tissue, and examine the material under a dissecting microscope. If desired, a fresh cover-glass preparation may be made and examined under higher magnification, or stained spreads or sections may be made. It is essential that one should be thoroughly familiar with the larval forms of the common trematode before undertaking the study of the life history of the parasitic trematodes of man.

Search for Trematodes in the Adult Stage.—The adult trematodes of the intestine in man may be found after the systematic administration of thymol to persons in whose feces the eggs have been seen. In this way Noc demonstrated the frequency of *Fasciolopsis buski* in Indo-China, and Garrison discovered *Fascioletta ilocana*. At autopsy, search for the parasite is made by carefully examining the digestive tract, liver, lungs, veins of the abdomen and pelvis, and in cases of schistosomiasis by examining the mesentery by transmitted light against a window or a bright light.

DIFFERENTIAL CHARACTERISTICS OF THE EGGS OF TREMATODES

	Differential characteristics	Average size in microns	Species	Source
Eggs operculated and relatively thin shelled.	Egg oval in shape, large in size, measuring 80 to 190 μ.	140 × 80	Fasciola hepatica.	Feces.
		179 × 85	Fasciola gigantica.	Feces.
		125 × 75	Fasciolopsis buski.	Feces.
		150 × 80	Fasciolopsis rathouisi.	Feces.
		100 × 60	Fascioletta ilocana.	Feces.
		150 × 72	Gastrodiscus hominis.	Feces.
		130 × 78	Cladorchis watsoni.	Feces.
		90 × 65	Paragonimus westermanii.	Sputum.
	Eggs small, measuring less than 50μ.	42 × 26	Dicrocelium lanceatum.	Feces.
		30 × 16	Clonorchis sinensis.	Feces.
		28 × 13	Opisthorchis felineus.	Feces.
		34 × 21	Opisthorchis noverca.	Feces.
		29 × 11	Metorchis truncatus.	Feces.
		25 × 16	Heterophyes heterophyes.	Feces.
Eggs non-operculated and relatively thick shelled.	Egg provided with terminal spine.	150 × 65	Schistosomum hematobium.	Urine.
	Egg provided with lateral spine.	150 × 60	Schistosomum mansoni.	Feces.
	Egg without spine.	75 × 40	Schistosomum japonicum.	Feces.

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CHAPTER XIV

CESTODA

GENERAL CONSIDERATION OF CESTODES

History.—Morphology and Structure.—Life History.—Mechanism of Transmission.—Habitat.—Pathogenesis.—Diagnosis.—Treatment and Prophylaxis.—Classification.

The cestodes are platyhelminthes (flat worms) having a segmented body and no alimentary canal at any stage in their life history. The adult parasite inhabits the intestine, and the larval form lives in the muscle, liver, brain, spleen, etc.

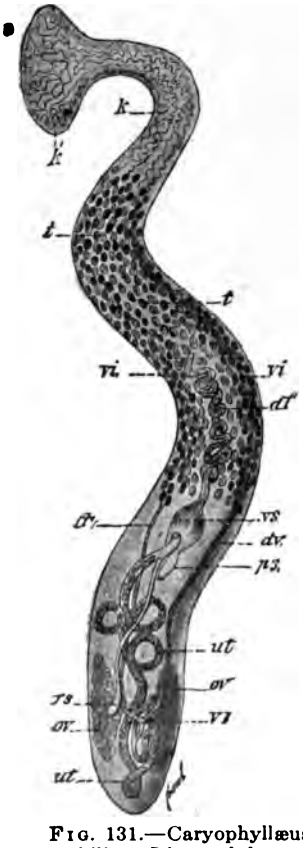


FIG. 131.—Caryophyllæus mutrabilis. *Df*, vas deferens; *dv*, vitelline duct; *K*, scolex; *ov*, ovaries; *ps*, penis; *vs*, vagina with receptaculum seminis; *t*, testes; *ut*, uterus; *vi*, vitellarium; *vs*, vesicula seminalis. (*After Shultze in Hertwig.*)

The majority of cestodes, more especially those found in man, are well differentiated from trematodes, but the boundaries between the two groups are less well marked in certain forms, such as *Caryophyllæus*, belonging to the Cestodaria, which are assigned by some to the trematodes and by others to the cestodes.

The most important characteristic features of the cestodes are: (1) All are endoparasites of the intestine in the adult stage and of the organs or tissues in the larval stage; also, as a result probably of their obligate and strictly parasitic existence, they have lost all traces of an alimentary canal. (2) They are nourished by the juices or the predigested food of the host through the body surface as the result of osmosis, for it is an open question whether the cuticle of the parasite is penetrated with pores for this purpose. (3) They present two distinct developmental stages in their life history, namely, the bladder worm, or *cysticercus*, in the organs (muscle, liver, brain, etc.), and the sexually mature parasite in the intestine of the host. (4) Division of the body of the adult into a head or scolex and a neck, followed by a series of segments or proglottides takes place. This last feature is true of all human tape-worms

and of the best known species. (5) Lime-secreting cells are present in greater or lesser number below the cuticle.

History.—There is sufficient evidence to lead us to believe that cestodes were known to the ancients, and that Moses forbade the Israelites to eat animals such as the hog, because of his knowledge of the parasites that were present in their flesh. Descriptions of the proglottides of tape-worms are found in the writings of Aristotle. In 1592 the Tenidæ were differentiated from Bothriocephalus. In 1683 Tyson discovered the head of the tape-worm of a dog, and in 1687 Redi detected the cysticerci, or bladder worms, which he regarded as animals. Zeder, in 1800, placed them in a separate group, *Cystici*. The nature and the life history of the cestodes were better understood when Küchenmeister, in 1851, proved, by feeding experiments, that the cysticerci merely represented the larval stage of tape-worms, and that to complete their life history two hosts were required. Among other investigators who have greatly increased and improved our knowledge of these parasites may be mentioned Leuckart, Braun, Looss, Sonsino, Grassi, Blanchard, von Linstow, Lühe, Stiles, Sambon, Leiper, and others.

Morphology and Structure.—In the adult stage the cestodes are divided into two groups: (1) The *Cestodaria*, commonly known as non-segmented cestodes, and (2) the *Cestoda* proper, which group comprises all forms possessing a head or scolex and segments or proglottides. It is the latter group that is of most interest in human parasitology.

The cestodes proper are recognized by their band-like or ribbon-shaped segmented body, which is white or pale yellowish in color. It is so suggestive of a long piece of tape that it is easy to understand how the common cestode worms come to be particularly called "tape-worms." The segments are distinct and broad posteriorly, but gradually become narrower and small anteriorly, until they finally merge into a constricted, delicate, non-segmented portion near the head known as the neck. A typical cestode, therefore, consists of three parts: The head or *scolex*, the *neck*, and the *body proper*, or *trunk*, made of numerous segments or *proglottides* (Figs. 132 and 142).

The Scolex.—The scolex or head is globular or pyriform in shape, and serves for attachment to the intestinal wall. The name of *strobile* is applied to the whole parasite, *e.g.*, head, neck, and proglottides. The attachment is accomplished either by means of muscular suckers (*Tenia saginata*), suckers and hooks (*T. solium*, *T. cracicalis* (Fig. 133), *etc.*), or by lateral grooves, or bothridia (*Dibothriocephalus latus*). When hooks are present, they are usually numerous, and arranged in one or two circular rows around a mammillary eminence at the tip of the head called the *rostrum* or *rostellum*. The hooks are curved out-

wardly and have the form of an angle, so that while they can easily penetrate the wall of the intestine, their detachment is accomplished with difficulty, and this explains why the head is not so easily detached when the worm is poisoned by medical treatment administered for its removal, and why it sometimes breaks off in removal at autopsy.

The Neck.—The neck is the non-segmented and narrowest portion of the parasite, connecting the head with the remainder of the body. It is somewhat cylindric in shape, and is of especial interest in the life of the parasite because it represents the vegetative portion from which new segments or proglottides are formed.

The body or trunk is made up of several segments or *proglottides*, their number varying from three to four in the smaller form (*Echinococcus granulosus*, *Tenia echinococcus*) (Fig. 132), to several hundreds or thousands in the large species (*T. saginata*) (Fig. 142). The proglottides near the neck are very small and indistinct, but gradually become larger and broader posteriorly, usually tapering at the end. This variation is dependent on the degree of maturation; thus, the first anterior segments are immature, and merely contain rudiments of the reproductive organs in the form of undifferentiated germ cells. Lower down, the male reproductive organs are first formed, and the rudiments of the female organs begin to appear, and at about the middle of the body the proglottides contain both mature males and female reproductive organs. Lower down still the male reproductive organs begin to degenerate and disappear, and in the older segments these are ab-

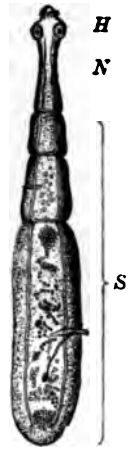


FIG. 132.

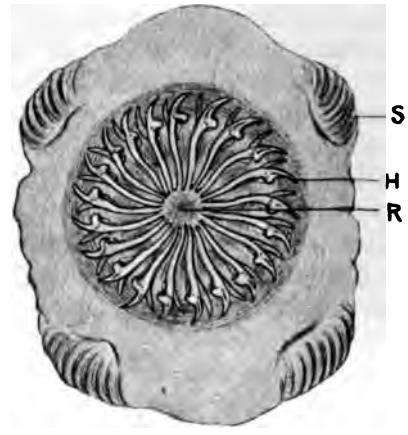


FIG. 133.

FIG. 132.—Tenia echinococcus. *H*, head; *N*, neck; *S*, segments × 15. (*After Leukart in Brumpt.*)

FIG. 133.—Head of Tenia crasicolis showing the suckers, *S*; and two circles of hooks *H*, attached to the rostellum *R*.

sent. When very old, the female reproductive organs also degenerate and finally only the uterus remains, appearing at times as a sac-like structure containing numerous eggs.

The Cuticle.—The cuticle (Fig. 134), which covers the surface of the parasite, consists of a very resistant, thick, homogeneous, non-chitinous substance, which is believed to be rich in lime salts. Beneath the cuticle is the subcuticle, or basal membrane, which is reticular in character, and made up of condensed parenchymatous tissue (Fig. 134). According to some authors, the cuticle is provided with pores for the interchange of fluids.

The Lime Cells.—The cestodes, either in the adult or in the larval stage, show the presence of lime cells or calcareous bodies immediately



FIG. 134.—Transverse section of the segment of a cestode, Tenia saginata. *Cu*, cuticle; *Scu*, subcuticle; *Lm*, longitudinal muscle fibers; *Cm*, circular muscle fibers; *P*, parenchyma; *Ut*, uterus; *E*, eggs.

below the subcuticle. These cells vary from 3 to 30μ in diameter, and are composed of concentrically arranged calcareous substance, soluble in acid, and inclosed in a cell having the nucleus at one side, and somewhat resembling a fat cell or starch grain. The function of these cells is not well understood: they may possibly represent a rudimentary skeleton, or, by neutralizing the acid of the surrounding medium, they may afford protection.

The Muscles.—The muscle consists of a delicate subcuticular layer, a longitudinal, and a circular or transverse layer. The transverse muscular layer is situated well into the parenchyma, and separates the cortical from the medullary portion of the parenchyma.

The Parenchyma.—The parenchyma constitutes the larger portion of the segment. It consists of cells, of embryonic type, spindle, globular, irregular, or ameboid in shape, and a reticular intercellular sub-

stance. It is divided into a cortical and a medullary portion, separated by the transverse or circular layer of muscles. In the cortical layer lie the sunken epithelial cells, nerve-cells, sense organs, excretory cells, etc., and a part of the reproductive organs. The medullary portion contains the greater part of the reproductive organs.

The Alimentary Canal.—In cestodes the alimentary canal is entirely absent.

The Nervous System.—The nervous system consists of a pair of cerebral ganglia, sometimes fused into a single mass, a nerve commissure, and two nerve cords which run laterally at each side throughout the whole length of the animal. In addition there are a pair of dorsal and a pair of ventral nerve fibers, which also extend through the entire animal and anastomose at different levels.

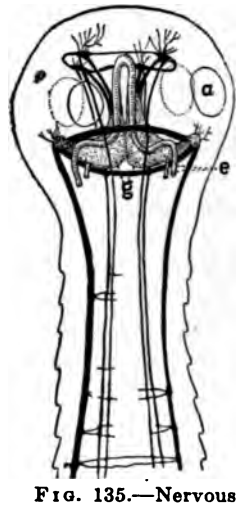


FIG. 135.—Nervous system of the cestode *Monesia*. *a*, Suckers; *E*, excretory tubes; *g*, cerebral ganglia. Newes black. (*After Tower in Hertwig.*)

Excretory System.—As in trematodes the excretory system in cestodes consists of a nephridial system of flame cells, with anastomosing capillaries which empty into the two collecting tubes at each side of the body. These tubes run from the scolex to the last proglottides, and anastomose at the posterior border of each segment by lateral channels. In the last proglottis the two lateral ducts unite into a common duct, which opens exteriorly into the excretory pore. In the original posterior proglottis there is a pear-shaped excretory vesicle, but as the last proglottides usually drop off, the excretory ducts empty separately at each side of the last segment.

The Reproductive Organs.—The reproductive organs in cestodes present a highly specialized form of development. All known cestodes are hermaphrodites, male and female reproductive organs being situated in each segment. The reproductive organs develop gradually as the proglottis matures; the male organs appear first and are followed by the female.

The Male Organs.—The male generative organs can best be studied in the segments between the middle and anterior part of the animal. They consist of numerous follicular *testes*, scattered over the dorsal portion of the medullary layer between the excretory ducts, although they may be grouped into one or several glands. Minute aberrant ducts are given off from each follicle, which unite, at about the middle of the proglottis, into a *vas deferens*. After running a wavy, convoluted course the vas deferens is continued by the *cirrus pouch*, and ends in the genital pore.

The Female Organs.—The female generative organs consist of a *vagina, receptaculum seminis, uterus,* and one, two, or more *ovaries.* The ovaries are usually two in number, and are situated ventrally, and at each side of the median line toward the posterior border of the segment. The ovaries are continued by the *oviducts,* which unite into a common duct which empties into the *oötype* below the receptaculum seminis. At this point it also receives the vitelline ducts, which convey the yolk secreted by the vitelline glands and the secretion from the shell gland, and is continued by the uterus. The receptaculum seminis is continued by the vagina, which ends in the genital pore at the side of the segment (*Teniidæ*), or anteriorly and

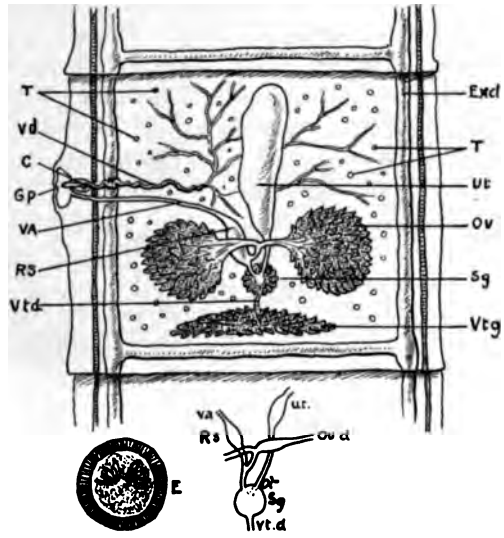


FIG. 136.—Diagram of the anatomy of a Tenia (*Tænia saginata*). *T*, testes; *Vd*, vas deferens; *C*, cirrus; *Gp*, genital pore; *Va*, vagina; *Rs*, receptaculum seminis; *Vtg*, vitelline glands; *Vtd*, vitelline duct; *Sg*, shell gland; *Ov*, ovaries; *Ovd*, oviduct; *Ut*, uterus; *Ot*, oötype; *Exd*, excretory duct.

ventrally, either in the middle or between the side and the median line (*Bothriocephalidæ*), as the case may be.

The uterus in cestodes may end in a culdesac; that is, it may have no external opening (*Teniidæ*), or may communicate with the exterior by a special opening, the *metraterm* (*Dibothriocephalidæ*). This latter feature makes possible the division of cestodes into two classes—those *without a birth pore* and those *with a birth pore,* respectively. Two types are, therefore, recognized. In the cestodes with a birth pore (*Dibothriocephalus*) the presence of vitellaria and a separate opening for the uterus and vagina recall the condition seen in the trematodes, whereas in the second group, those without the birth pore (*Teniidæ*), the uterus ends blindly and the vitellaria are modified

into small albumin glands. Reference should be made in this connection to the Laurer's canal in trematodes, which may be said to represent the vagina in cestodes.

The difference in the sexual organs exerts an influence on the peculiarities of the egg. Thus in *Dibothriocephalus* the egg is large, operculated, and incloses a small egg cell and numerous yolk-cells, as in trematodes. The eggs of *Teniæ* are small, with a layer of albumin and a delicate shell, which is lost early and replaced by an embryonic shell or radially striped envelop called an *embryophore*. The latter is not operculated, and is formed by the embryo in an advanced stage of development. This is the stage in which the eggs of *Tenia* are found in the feces.

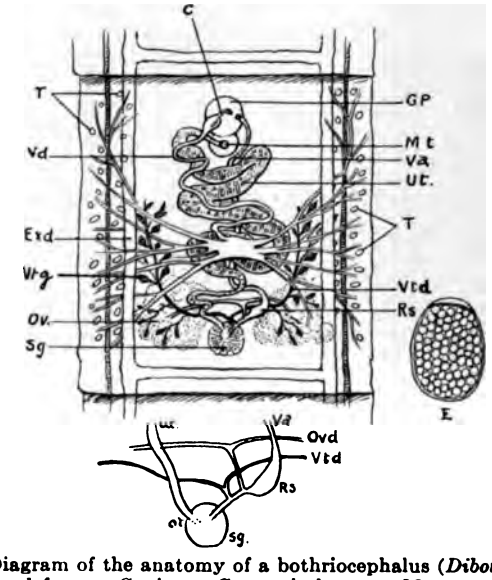


FIG. 137.—Diagram of the anatomy of a bothriocephalus (*Dibothriocephalus latus*) *T*, testes; *Vd*, vas deferens; *C*, cirrus; *Gp*, genital spore; *Mt*, metraterm; *Va*, vagina; *Ut*, uterus; *Rs*, receptaculum seminis; *Ov*, ovaries; *Ovd*, oviduct; *Vtg*, vitelline glands; *Vtd*, vitelline duct; *Ot*, oötype; *Sg*, shell gland; *Exd*, excretory duct.

A further difference is that in *Dibothriocephalus*, as in the trematodes, the egg must enter water for its further development; here it gives rise to a ciliated and hooked larva (*onchosphere*), which enters a fish, where it undergoes still further development. In *Tenia*, on the other hand, the hooked larva is freed by the digestion in the stomach of the proper intermediate host, bores its way through the walls of the intestine, and migrates through the lymphatics and blood-stream into the muscles or other organs, where it becomes encysted and undergoes further development.

Function.—The testes give rise to the sperm cells, which, carried by the vas deferens and the cirrus, are discharged into the vagina and

collect in the receptaculum seminis. The ovaries give rise to the egg cell, which, after fertilization in the oviduct, passes to the oötype, where it receives the yolk or reserve food material from the vitelline gland and the secretion from the shell gland, from which the shell of the egg is formed. The egg now enters the uterus, and in *Tenia* undergoes development, so that, as found in the uterus or when discharged with the feces, it usually contains a hooked larva called an *onchosphere*. In *Dibothriocephalus*, as in the trematodes, the development of the egg may begin in the uterus, but it is usually completed outside, so that, as discharged with the feces, it generally consists of a single cell.

Life History.—As the male and female apertures are so close to each other in the genital opening, self-fertilization may occur, with or without the aid of the cirrus, or if, by chance, two proglottides should come in contact, cross-fertilization may take place. In either case the sperm cell passes through the vagina into the receptaculum seminis. Fertilization usually takes place near the oviduct, after which the egg passes to the oötype, where it receives the yolk (*Dibothriocephalus*) or albumin (*Tenia*) secreted by the vitelline glands, and the shell from the shell gland, and passes into the uterus, from which it may escape through the birth pore (*Dibothriocephalus*). If no birth pore is present (*Tenia*), the egg is retained in the uterus until the proglottides are destroyed. Further development in the two families of cestodes differs so much in certain essential features that *Dibothriocephalidæ* and *Teniidæ* will each be considered separately.

Development of Dibothriocephalus (Plate VIII).—The fertilized egg as found in the feces is relatively large, oval in shape, and brown or yellowish in color. Taking *Dibothriocephalus latus* as a type, the egg is 70μ in length by 45μ in width. Like most trematodes, the egg of *Dibothriocephalus* is provided with a relatively thin shell, operculated at one pole, and usually containing one or few cells at the center, surrounded by numerous yolk cells.

Development begins in the uterus, and is completed outside, in water. It usually takes place gradually, consuming some months under normal conditions, or within ten to fifteen days at a temperature of 30° to 35° C. for the formation of the onchosphere (Schauinsland). The egg cell first divides, and gives rise to two, then to four, and finally to a mass of cleavage cells. By differentiation these cleavage cells give rise to an outer layer of cells, the ectoblast, and an inner group of cleavage cells, the entoblast. The entoblast finally forms a six-hooked larva, and the cells of the ectoblast develop cilia.

The ciliated larvæ now escape through the operculum, become free, and swim about freely in water for several days. It is probable that, in this stage, as with the miracidium in trematodes, the larva enters

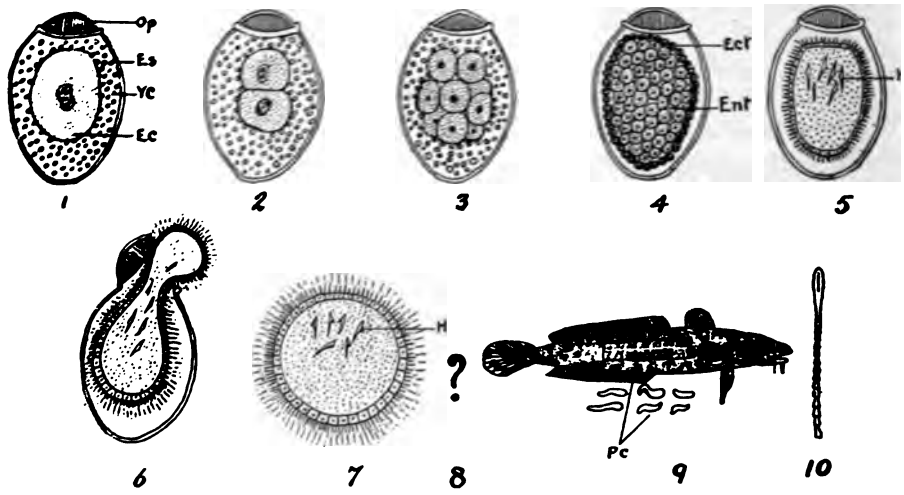


PLATE VIII

Diagram of the life history of a bothriocephalus (Dibothriocephalus latus).

1. Fertilized egg. *Op*, operculum; *Es*, egg shell; *Yc*, yelk cells; *Ec*, egg cell.
2 and 3. Cleavage stages.
4. Differentiation of ectoblast *Ect*, and entoblast, *Ent*.
5. Hooked and ciliated larva within the egg shell. *H*, hooks.
6. Ciliated larva escaping through the operculum.
7. Free ciliated larva (first larval stage).
8. Probably an unknown stage in some invertebrate host (?).
9. Fish infested with the plerocercoid *Pc* (second larval stage), shown in the muscle and free below.
10. Scolex of *Dibothriocephalus latus* about normal in size.

an unknown invertebrate host, loses the ciliated ectoderm, becomes ameboid, and undergoes development and probably encystment. In this stage it most likely enters the salmon (*Salmo umbla*), trout (*Trutta vulgaris*), or other fish. In the muscle or viscera of the fish as demonstrated by Max Braun, it is transformed into a *plerocercoid*, which, when swallowed, develops directly, in the intestine of the host, into the scolex of a Dibothriocephalus.

The plerocercoid larva is easily seen with the naked eye. It is white in color, and measures 1 to 2 cm. in length by 2 to 3 mm. in width. It is more common in the viscera of the fish than in the muscle. Like all cestode larvæ, it is destroyed in a few minutes at 50° C., at −3° to −1°C., and also in strong salt or acid solution. Man becomes infested by eating underdone or raw fish in the form of caviar. On reaching the intestine, the plerocercoid larva attaches itself to the wall by means of the *bothridia* (two lateral grooves at each side of the head). It attains the adult stage in about five or six months, eggs are discharged, and the cycle is repeated.

Development of Tenia (Plate IX).—In Tænia the development of the fertilized egg begins in the uterus, but as the egg is not discharged, further development proceeds in the uterus to the advanced stage, called *onchosphere*. The process is similar to that described for *Dibothriocephalus*, except that in *Tenia the onchosphere is not ciliated and does not hatch outside*. The mode of development is as follows: After fertilization the egg cell receives the yolk or albumin and the shell from the vitelline gland and shell gland respectively. The egg cell now divides, forming four cells, one of which, by division, gives rise to a membrane—the *hull membrane*—while the remaining three cells divide and form a mass of cleavage cells. This mass of cleavage cells now becomes differentiated into ectoblast (not ciliated) and entoblast, the latter finally giving rise to a hooked larva. In its development, therefore, the embyro gives rise to two membranes—an outer one, in contact with the egg shell—the *hull membrane*—and an inner one or ectoblast, in contact with the embryo—*the embryophore*. The original egg shell and the outer or hull membrane are soon lost, and the egg, as it appears in the feces, is surrounded by this embryonic inner membrane, or *embryophore*, which is pierced by fine channels for the interchange of fluids, and contains an embryo provided with six hooks and called an *onchosphere*.

In some *Teniæ* the embryophore is surrounded by a large, irregular, and clear zone, a capsule or cyst-like structure called the amnion (*T. solium*), seen especially in fresh specimens directly prepared from the uterus by teasing the segment in a little water; this is rarely, however, found in the feces. It is therefore evident that the so-called

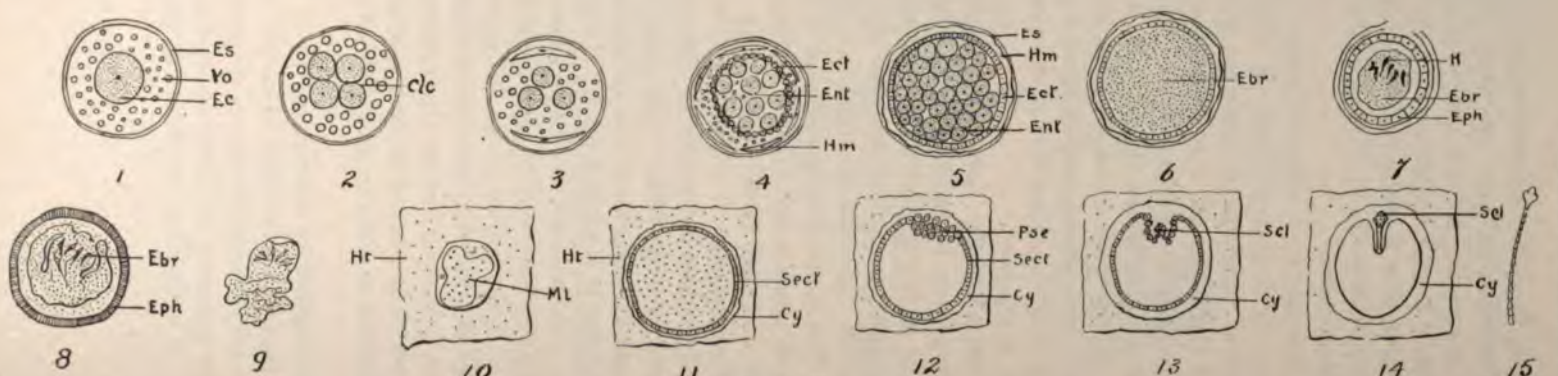


PLATE IX

Diagram of the life history of a tenia (Tenia saginata). 1. Fertilized egg: *Es*, egg shell; *Yc*, yolk cells; *Ec*, egg cell. 2. Cleavage, four cell stage. *Clc*, cleavage cells. 3. One of the cleavage cells, by division, giving rise to the hull membrane. 4. Hull membrane, *Hm*, almost formed and cleavage cells differentiating into ectoblast *Ect*, and entoblast, *Ent*. 5. Ectoblast, *Ect*, entoblast, *Ent* and hull membrane *Hm*. Well defined. 6. Entoblast giving rise to an embryo *Ebr*. 7. Hooked embryo formed and egg shell and hull membrane being cast off. *H*, hooks; *Eph*, embryophore. 8. Onchosphere as it appears in the feces. 9. Hooked larva free in the intestine, ready to pehetrate the mucosa. 10. The metamorphosed larva, *Ml*, an ameboid body, lodged in the host tissue *Ht*. 11. Secondary ectoblast, *Sect*, formed and production of a cyst, *By*, by the host tissue. 12. Proliferation of secondary ectoblast, *Pse*, at one pole. 13. Invagination of secondary ectoblast and formation of scolex. 14. Fully formed cysticercus with scolex evaginated. 15. Scolex, about normal in size.

egg in cestodes, as found in the feces, is not an egg, but the *onchosphere*, or embryo egg stage in the development of the parasite.

For their further development the cestodes generally require another host. When swallowed by a susceptible host, the onchosphere, on entering the alimentary canal, casts off the embryophore, and the larva, being set free, makes its way by means of the hooks through the walls of the intestine into the tissue, when it casts off the hooks, and on reaching the blood-stream is carried to various parts of the body. On reaching a suitable tissue or organ it takes on an ameboid shape, becomes encysted, and by asexual reproduction gives rise to the formation of a scolex. The development proceeds as follows:

On reaching a suitable organ or tissue, such as the liver, muscle, etc., the larva lodges in the tissue, becomes ameboid, and undergoes metamorphosis and development, finally giving rise to the formation of a secondary ectoblast. This causes a stimulation or irritation of the surrounding tissue, and as a result a cyst is formed by the host around the developing embryo. At a certain point the secondary ectoblast, by proliferation, gives rise to a thickening, which, by becoming invaginated, forms the origin of the future scolex. When a more advanced stage of development is reached, the head develops a sucker (*T. saginata*) or sucker and hooks (*T. solium*), as the case may be. The scolex now grows and elongates inside of an embryonic cyst or bladder, hence the name, "bladder worm," given to the parasite at this stage.

If the larva forms a bladder-like cyst, it is called *cysticercus* (*T. solium*); if small and almost free from liquid, *cysticercoid* (*Tenia nana*), and if it has a caudal appendage it is termed *cercocystis*. The name *hydatid* is commonly applied to the encysted larvæ of *Equinococcus granulosus* (*T. echinococcus*). In the case of *Dibothriocephalus*, as previously stated, the onchosphere develops into a scolex in the shape of an elongated larva, which is not encysted and is called *plerocercoid*.

As a rule, in the hydatid or cysticercus stage the larva does not undergo further development and differentiation until it enters another and a different host. *Hymenolepis nana*, however, may undergo its larval stage in the villi of the intestine of the rat and its adult stage in the lumen of the same host (Grassi).

On being swallowed by a susceptible new host, the cyst is digested or drops off, the scolex attaches itself to the wall of the intestine by means of the sucker or the suckers and the hooks, as the case may be, and in a few weeks the process culminates in the development of an adult tape-worm. In time either the onchospheres (eggs) or the mature proglottides filled with them are discharged externally, and

when these are swallowed by a susceptible host, the onchospheres are liberated and penetrate the intestinal wall, and the cycle is repeated.

The time occupied in the development of an onchosphere into a cysticercus is from two to six months or more; in the development from the cysticercus to the adult tape-worm a few weeks are consumed. The span of life of an adult tape-worm is not known, but it is probably very long—five years or more—according to the vegetative powers of the scolex. Abnormalities or monstrosities are often encountered in cestodes.

Asexual Development by Budding.—The bladder-worm stage (cysticercus) of certain cestodes, such as *T. solium* and *T. saginata*,

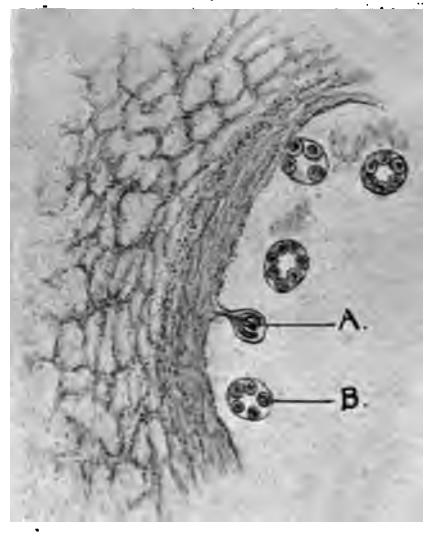


FIG. 138.—Hydatid cysts in the lung of a camel showing Scolices or hydatids, *A* attached to the cyst wall and free in the cavity of the cysts *C*.

usually consists in the development of a single cyst containing a single larva; that is, each onchoshpere gives rise to a single larva or scolex. In other cestodes, however, such as *Cenurus cerebralis*, which lives in the brain of the sheep, several scolices are produced and the number is even greater in *Equinococcus granulosus* (*T. echinococcus*), in which the cyst increases in size, producing a tumor-like growth, which, when located in the liver, may weigh from ten to thirty pounds. This extraordinary size is explained by the increase in the size of the mother cyst and the production, by budding, of secondary or daughter cysts, also called *vesicula proligera*, before the formation of scolices begins, as is the case with *Canurus cerebralis*. In

Equinococcus granulosus, in addition, a number of brood vesicles or grand-daughter cysts emerge from the interior of each daughter cyst, and these, by invagination, give rise to numbers of scolices. Thus from a single onchosphere thousands of scolices may arise from the daughter cysts or vesiculæ proligeræ. This is a striking example of pedogenesis (Fig. 138).

Cestodes, like trematodes, furnish biology with one of the most remarkable examples of vegetative reproduction in animals and the proliferative capacity common to parasites in general. Dévé has

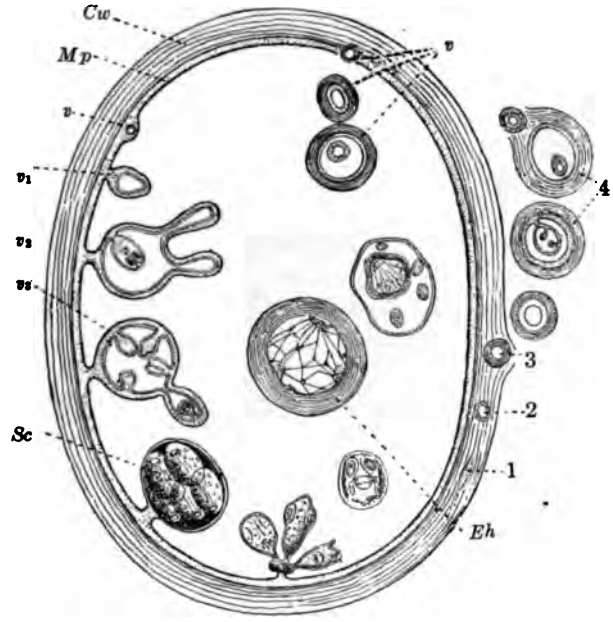


FIG. 139.—Hydatid cyst. *Cw*, cyst wall; *Mp*, membrana proligera; *v* and v_1, endogenous formation of a daughter cyst; v_2 and v_3, endogenous formation of grand daughter cysts; *Sc*, scolices; *Eh*, endogenous hydatid (Scolex) free inside of the cyst; 1, 2, 3, 4, mode of formation of exogenous daughter cyst. (*After R. Blanchard in Brumpt.*)

estimated that 1 c.c. of the sediment collected from the liquid of a hydatid cyst contains about 400,000 scolices, and as a fertile cyst may furnish from 3 to 6 c.c., the number of scolices in a cyst may number about 2,000,000. It has also been estimated that as the number of eggs in the adult worm may number from 400 to 800, a single parasite may, therefore, give rise to about 1,000,000,000 scolices.

Endogenous and Exogenous Cysts.—The daughter cyst or vesicula proligera is formed by budding through a proliferation of the inner lining of the mother cyst, *membrana proligera*, and the buds are usually *endogenous* in formation, but occasionally they may be exogenous and invade the surrounding tissue.

Unilocular and Multilocular Cysts.—The development of the onchosphere of *Equinococcus granulosus* (*Tenia echinococcus unilocularis*) in the liver, for instance, is the cause of a chronic inflammatory reaction, poorly limited, which gives rise to the formation of a cyst surrounded by a fibrous capsule, called the host membrane or *membrana adventitia*, within which numerous hydatids or scolices are formed as described. The collective structures formed by this reaction, namely, the cyst and the larvæ within the cyst, constitute a *hydatid cyst*, which may be either unilocular or multilocular.

Unilocular Hydatid Cyst.—The unilocular cyst usually consists of a single cavity, limited or encapsulated by the host membrane, but two or more may exist independently of each other. It may be either primitive or secondary in origin.

Primitive Unilocular Hydatid Cyst.—The primitive cyst is the one formed by the original larva. It varies in size, according to the degree of development, and although usually single, two or more primitive cysts may be found in the same organ. This is due probably to the simultaneous development of two or more onchospheres at the time of the infection or to subsequent reinfection.

Secondary Unilocular Hydatid Cyst.—A secondary unilocular hydatid cyst is an independent structure, derived from the original, due to the escape of hydatids or scolices, which, when set free, are capable of giving rise to the formation of new cysts in the surrounding tissues or organs. The secondary unilocular cyst, therefore, is derived from the same primitive larva, and should be regarded as a graft or daughter cyst from the mother cyst. The causes of this secondary cyst formation are: (1) Spontaneous rupture of an old abdominal hydatid cyst (hepatic, splenic, etc.) into the peritoneum, which, according to Dévé, occurs in about 22 per cent. of the cases observed in the liver. (2) Incomplete or imperfect removal of the cyst by surgical intervention. (3) The result of exploratory or evacuative puncture of the cyst, which allows the escape of the liquid and the scolices into the peritoneum.

Multilocular Hydatid Cyst.—The multilocular hydatid cyst is believed to be caused by *Echinococcus multilocularis* (*Tenia echinococcus multilocularis*), a parasite resembling *E. granulosus*, but distinguished from it by the peculiar formation of numerous cysts or chambers that usually communicate with one another. These, by infiltrating the surrounding tissue, give rise to a growth which is neoplastic in nature and somewhat ulcerative in character. The formation of this multilocular cyst is accomplished by a marked prolongation with infiltration of the primitive protoplasm of the *vesicula proligera* into the surrounding tissue. These prolongations are ameboid or plasmodium-like. When young, they invade the surrounding tissue and even the blood-vessels and lymphatics, and as the

cularization of these prolongations does not appear except secondarily, this would tend to explain the formation of the numerous and small vesicular cavities ramified in all directions that characterizes the *Echinococcus multilocularis*.

Mechanism of Transmission.—As man may be either the primary or the secondary host of cestodes, infestation is dependent upon the species of parasite. Thus the *plerocercoid* represents the infective stage of *Dibothriocephalus latus*, and man is infested by eating improperly cooked fish infected with the larva of the parasite. Infestation by *Tenia solium* and *T. saginata* takes place by eating improperly cooked pork or beef respectively, the meat being infested with parasites in the bladder-worm stage (*Cysticercus cellulosa* or *C. bovis*). On reaching the intestine, the larva, as in *D. latus*, grows into an adult



FIG. 140.—Echinococcus multilocularis in the liver of man. Natural size showing the honey-comb appearance and absence of encapsulation of the cyst. (*After R. Blanchard in Brumpt.*)

parasite. In the case of *Echinococcus granulosus* and *E. multilocularis*, in which man is the secondary host of the parasite, infestation takes place by the ingestion of water or food contaminated with the onchospheres, or by coming in contact with dogs and other infested animals. On being set free in the digestive tract, the onchospheres penetrate the walls of the intestine, reach the blood-stream, and when lodged in the proper organ (liver, spleen, etc.), develop into hydatid cysts.

Habitat.—The adult cestodes are, without exception, parasites of the intestine of man or of lower animals, the larvæ or cysticerci living in the tissues or internal organs. The life history of all cestodes, as a rule, requires two hosts, and man may be either the primary or the secondary host, as the case may be. Thus in infection by *Tenia solium*, *T. saginata*, *Dibothriocephalus latus*, etc., man is the primary host, in *T. echinococcus*, he is the secondary host.

The bladder-worm stage or hydatid cyst of *Echinococcus granulosus* in man is found in the liver in over 50 per cent. of the cases. Other organs also affected, in the order of their frequency, are: lungs, peritoneum, muscles, kidneys, pelvis, genital organs, neck, mesenteric glands, and brain.

Pathogenesis.—The morbid changes brought about by the presence of cestodes depend upon whether or not man is infested with the adult parasite, or with its larva, and also upon the degree of infestation. It happens, sometimes, that the presence of a single *Tenia* may not give rise to any appreciable symptoms, but, as a rule, in multiple infestation, gastro-intestinal disturbance and a certain degree of anemia are present. This is especially true of *Dibothriocephalus latus*, which usually gives rise to a pernicious form of anemia.

In the case of hydatid cyst, the symptoms depend, in large part, on the degree of infestation, the size of the cyst, and upon the organ affected. Thus, although a hydatid cyst of the liver may not give rise to a marked disturbance, it is, as a rule, the source of grave symptoms, which, when localized in the brain, usually terminate fatally. In general cachexia, anemia, and eosinophilia are common to cestode infestation, and, in addition, other symptoms, related to the part affected, may be present, such as gastro-intestinal disturbances in infestation with the adult worm, hepatic or pulmonary symptoms in hydatid cyst of the liver or lungs, respectively, etc. The symptoms of a hydatid cyst of the brain resemble those of cerebral tumor, and consist of vertigo, syncope, convulsions, vomiting, motor and sensory disturbances, softening, apoplexy, and coma, with, as a rule, a fatal termination.

Diagnosis.—The symptoms produced by the presence of adult tapeworms in the intestine are so varied and inconstant that the diagnosis must be based chiefly upon the finding of the eggs or of segments of the worm, or both, in the feces. In the case of *Dibothriocephalus latus*, in which, as in trematodes, a birth pore exists, the eggs are usually found in the feces. These are operculated, oval in shape, brown or yellowish in color, and measure 70μ by 45μ. In *Tenia solium*, *Tenia saginata*, and other *Teniæ* in which there is no birth pore and the eggs are retained in the uterus, the feces should be examined for the presence of detached segments, but as the proglottides are generally broken before they are discharged, the eggs may also be found in the feces. The eggs of *Tenia solium* and *Tenia saginata* resemble each other so closely that a diagnosis to be made with certainty, must sometimes be based upon the finding of the segments, which as described in the next chapter, present characteristic differences.

The diagnosis of hydatid cyst is a more complex problem, especially when the cyst is located in the brain, when it may be mistaken for

syphilis, cerebral tumors, epilepsy, etc. The diagnosis of hydatid cyst of the liver, lung, pelvis, etc., is likewise made with difficulty, especially in the early stages; a study of the symptomatology of echinococcus infestation will disclose the multiplicity of diseases with which this condition may be confused.

Briançon's sign, or "hydatid fremitus," is regarded as pathognomonic of hydatid cyst. This fremitus is elicited by applying one hand over the cyst, using moderate pressure, and percussing with the other hand over the tumor. On performing auscultation a grave vibrating sound may be heard. This sound is similar to that obtained by repeating this operation while holding on the palm of the hand several hydatids or a mass of gelatin. Briançon's sign, however, is applicable only to a few cases (liver and pelvis) in which the tumor is easily palpable and, moreover, it is not constant.

In general it may be said that a patient presenting a tumor (which may or may not yield the hydatid fremitus), accompanied by a certain degree of anemia and eosinophilia, and who has occasional attacks of urticaria, should be suspected of having an echinococcus infestation. On section of the tumor, the hydatids or scolices may easily be recognized.

Serum Diagnosis.—Either the precipitin or the complement-fixation test may aid in formulating the diagnosis. The precipitin test is performed by incubating a mixture of equal parts of the fluid of a hydatid cyst and the serum of the patient at 37° C. A positive reaction is indicated by cloudiness of the mixture. It is essential that a control test should be made at the same time, employing the fluid of the hydatid cyst and normal serum. In case of suspected infestation with *Dibothriocephalus latus, Tenia solium, T. saginta, etc.*, the reaction is obtained by using an extract of the adult worm in question. The precipitin reaction is positive in about one-third of the cases.

The complement-fixation test is made in the same manner as the Wassermann reaction for syphilis, using as antigen the fluid of the hydatid cyst or an extract of the adult worm, as the case may be, previously titrated. (See the following chapter and Chapter XXX, on Complement Fixation.)

Finally the microscopic diagnosis is made by centrifugalizing the fluid of a hydatid cyst (after digestion with antiformin or a 10 per cent. NaOH solution if required) and finding the scolices or hooks in the sediment.

Treatment and Prophylaxis.—A large number of remedies have been recommended for effecting the expulsion of the adult tape-worms from the intestines. Among these are male-fern, pelletierin, thymol, etc., each of which may give good results in certain cases, but their

action is not constant. It may be said, therefore, that there is no specific for the successful treatment of these parasites. The remedies, as a rule, act as irritants, and probably have a toxic effect on the worms, with the result that they lose their grip on the intestinal mucosa and are carried away by the peristaltic movements of the intestine, especially if the remedy employed is followed by a purgative. Not uncommonly the worm is expelled during an attack of severe diarrhea or following the administration of a laxative, which points to the fact that a change in the chemistry of the intestinal canal and the mechanical action of the peristalsis of the intestine are essential for the successful expulsion of the parasite. It is probably to this, more than to any specific action of the drug, that the beneficial effect of thymol and other remedies used in the treatment of intestinal parasites is due.

Not infrequently intestinal parasites have been known to be expelled during the course of infectious fevers, especially when these are accompanied by high temperatures. As previously stated, this is an example of the detrimental effect of physicochemical agents upon the parasite. It is highly improbable that the infectious fevers exert any especial antagonistic effect upon the parasite beyond that produced by the high temperature. It seems, therefore, that *any drug or agent that will maintain, for a certain time, an alteration of the physicochemical properties of the intestinal tract, but which at the same time does not give rise to marked disturbances in the host, is the logical remedy to use in the treatment of cases infested with the adult parasite,* especially if this remedy is augmented by mechanical aids, such as the production of an increased peristalsis by the administration of a purgative.

No treatment can be counted as successful unless it is followed by the expulsion of the head of the worm. If the head is retained, it will, in the course of time, give rise to the formation of new proglottides, and in such cases treatment must be repeated in about three months time. It may happen, however, that on account of the small size of the head, it may not be detected in the dejecta. No case should be regarded as cured until neither eggs nor segments can be found in the feces for a period of not less than three months following treatment.

The hydatid cysts are sometimes treated by simple puncture or aspiration of the fluid, followed by the injection of a parasiticidal substance, as, *e.g.*, formaldehyde, 1:100. This procedure should be condemned, as a secondary bacterial infection and suppuration may ensue, or secondary cysts may form from the scolices, which may accidentally have fallen into the peritoneum during the operation. The surgical treatment to be recommended is complete removal of the cyst contents and the membrane proligera when possible, care being taken during the operation to avoid the escape of the contents of the cyst.

Prophylaxis.—To be effective, the prophylactic regulations require a thorough knowledge of the life history, and more especially of the mechanism of transmission, of the parasite. Thus, as the infective stage of *Tenia solium* is the cysticercus, commonly found in the muscle of pork; that of *Tenia saginata*, the cysticercus, found in beef; and that of *Dibothriocephalus latus*, the plerocercoid, found in fish, etc., care should be taken to avoid the ingestion of these foods when improperly cooked. In *Echinococcus granulosus* the infective stage is the onchosphere or egg, as found in the feces of the dog and other animals; contact with these infested animals should, therefore, be avoided.

Classification.—The classification of cestodes is based upon such morphologic differences as the presence or absence of suckers, bothridia, rostellum, hooks, and birth pores (metraterm or uterine orifice); position and number of genital pores in each segment; shape and disposition of the uterus; form and size of the egg, etc.

The classification generally followed is that of Monticelli given by Braun. The first-named author divided the parasites into two subclasses: I. *Cestodaria* (Monticelli, 1892), and II. *Cestoda sensu strictu* or cestodes proper (Monticelli, 1892). This division is based on the absence of segments in the former and the differentiation of the adult worm into head and proglottides in the latter.

I. **Cestodaria.**—The Cestodaria are trematodiform cestodes consisting of a single segment, which, like the trematodes, usually contains a single set of male and female reproductive organs. The group is divided into two families.

Family 1. *Caryophylleidæ.*—Cestodes resembling trematodes, consisting of a simple sexual apparatus. The body is made up of a single segment (scolex and proglottis not differentiated), distinguished from the trematode by the absence of a digestive tract. In this respect, therefore, they may be regarded as a connecting link between cestodes and trematodes (Fig. 131). The larval stage is found in an invertebrate, and the adults are usually found in fish. Thus *Caryophylloeus* is found in the intestine of *Cyprinoides amphilina*, in the body cavity of sturgeon; *Archigetes*, in anelids.

Family 2. *Ligulidæ.*—This family is provided with numerous sexual organs, but the scolex and proglottides are not differentiated. The immature stages are found in the body cavity of fish; the adult, in the intestine of birds (*Ligula*).

II. **Cestodes Proper** (*Cestoda sensu strictu*).—This group comprises the typical cestodes, and is recognized by the differentiation of the adult worm into scolex and proglottides or segments, which may vary from two or three (*Tenia echinococcus*) to several thousand (*Dibothriocephalus latus*) in number. Each segment is provided with complete

male and female reproductive organs. The group is divided into five families:

Family 1. *Trypanorhynchidæ* (Diesing).—Synonym; *Tetrarhynchidæ*. Scolex with two to four bothridia and four protrudible and long rostella, armed with hooks. They are parasites of fish, *Rhynchobothrium bisulcatum*.

Family 2. *Tetraphyllidæ* (Carus).—Scolex provided with four very mobile suckers, often armed with hooks; no uterine orifice. *Echinobothrium variabile*.

Family 3. *Diphyllidæ* (Carus).—Scolex provided with two bothridia, a rostellum, and hooks.

Family 4. *Pseudophyllidæ* (Carus, 1863).—Synonym: *Bothriocephalidæ*. Scolex armed or unarmed, and with two lateral grooves like suckers. Birth pore present. Eggs with or without operculum.

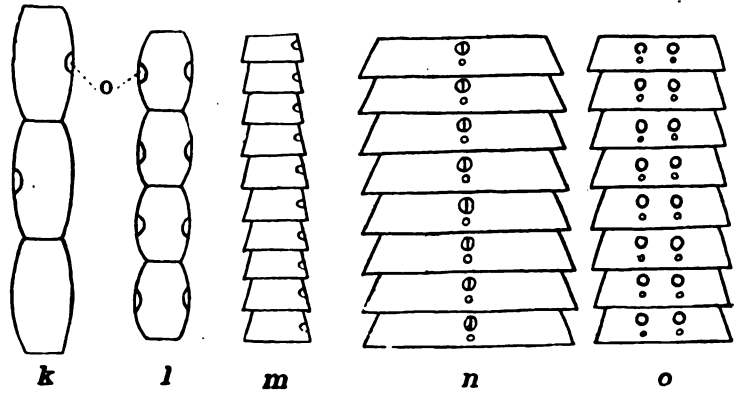


FIG. 141.—Diagram of the location of the *genital pore O*, of cestodes. *K*, Tenia; *L*, Dipylidium; *M*, Hymenolepsis and Davainea; *N*, Dibothriocephalus; *O*, Diplogonophorus. (*After Neveu-Lemaire in Brumpt.*)

Family 5. *Cyclophyllidæ* (Van Beneden).—Synonym: *Teniidæ*. Scolex provided with four suckers and an apical rostellum, with or without hooks. Uterine orifice or birth pore is absent. Eggs have no operculum.

The two families *Bothriocephalidæ* and *Teniidæ* are the only ones of interest in human parasitology, as they embrace the parasitic cestodes of man.

Bothriocephalidæ.—These worms are characterized by the fact that the scolex is provided with two lateral grooves or *bothridia*. The genital pore may be single, and situated at the middle of each mature segment (*Dibothriocephalus*); or it may be double, and situated on each side of the median line (*Diplogonoporus*). The genital pore contains three orifices—the male and female aperture for copulation. and the metraterm, birth pore, or uterine orifice, for the discharge of the egg. The egg is operculated, and gives rise to an onchosphere,

which is not formed in the uterus, but externally in water, where it hatches into a ciliated larva resembling the miracidium of trematodes.

Teniidæ.—These worms are characterized by the fact that the scolex is provided with four suckers. The birth pore is absent and the genital pore which opens at the side of the mature segment contains only the male and the female opening. The uterus is a closed sac, having no outlet, and consequently the eggs are not discharged except when the cuticle of the proglottides is broken and the segment disinte-

CLASSIFICATION OF THE PARASITIC CESTODES OF MAN

Order	Family	Differential Characteristics	Genus	Species	Size
I. *Pseudophyllidea.* Head with two groove-like suckers. Genital pore with three orifices. Birth pore present. Eggs usually operculated.	I. *Dibothriocephalidæ.* Proglottides distinct and drop off in groups. Uterus forms a roset. Single or double set of genital organs.	Single set of genital organs. Genital pore on the midline of segment. Eggs operculated.	Dibothriocephalus.	*D. latus;* *D. cordatus;* *D. parvus.*	2–20 m. 1 m.
		Double set of genital organs. Genital pore at each side of the midline of each segment.	Diplogonoporus	*D. grandis;* *D. brauni.*	10 m. 29 cm.
		Plerocercoid: adult not known.	Sparganum.	*S. mansoni;* *S. prolifer.*	
	2. *Ligulinæ.* Trematodiform.	External segmentation not marked; neck absent.	Braunia.	*B. jassyensis.*	18 cm.
II. *Cyclophyllidea.* Head with four suckers. Rostellum with or without hooks. Birth pore absent. Eggs not operculated.	*Taniidæ.* Genital organs single or double.	Adult worm very long. Larval stage or cysticercus containing a single scolex. Genital pore alternating Head with or without hooks. Mature segment usually much longer than wide.	Tenia.	*T. solium;* *T. saginata.*	3 to 8 m. 4–10 m.
		Adult worm small. Head with rostellum and hooks. Genital pore alternating. Larval stage a hydatid cyst containing numerous scolices.	Echinococcus.	*E. granulosus;* *E. multilocularis.*	2.5–6 mm.
		Head with or without hooks. Genital pores on the same side of each each proglottis; segment small and much wider than long.	Hymenolepis.	*H. nana;* *H. diminuta;* *H. lanceolata.*	10–40 mm. 20–60 cm. 3–13 cm.
		Head with hooks. Genital pore on same side or irregularly alternating on each segment.	Davainea.	*D. madagascariensis;* *D. asiatica.*	25–30 cm. 30 cm.
		Head with hooks. Genital pore double on each segment. Mature proglottides much longer than wide.	Dipylidium.	*D. caninum.*	15–40 cm.

grates. As a result of the prolonged retention of the egg in the uterus, when it is liberated, the onchosphere is already formed, and when swallowed by a susceptible host, is capable of direct evolution. Certain species of this family, such as *T. solium*, *Hymenolepis nana*, *T. saginata*, and *Echinococcus granulosus*, are common parasites of man; others, as *Dipylidium caninum* and *Hymenolepis diminuta*, are common to the lower animals, and are only occasionally found in man.

The chief differential characteristics of the parasitic cestodes of man are given in the accompanying table:

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CHAPTER XV

CESTODA (Continued)

THE PARASITIC CESTODES OF MAN

Dibothriocephalus latus; D. cordatus; D. parvus; Diplogonoporus grandis; D. brauni; Sparganum mansoni; S. prolifer; Braunia jassyensis; Tenia solium; T. saginata; Echinococcus granulosus; E. multilocularis; Hymenolepis nana; H. diminuta; H. lanceolata; Davainea madagascariensis; D. asiatica; Dipylidium caninum.—Other Cestodes.—Laboratory Diagnosis of Cestodes.

1. Dibothriocephalus latus (Bremser, 1819).—The adult worm is yellowish gray or whitish in color, and from 2 to 15 or even 20 meters in length. It is made up from 3000 to 4000 segments. The head is elongated, somewhat pear shaped, measuring about 2.5 mm. in length, and is provided with two grooves or suckers—one ventral and the other dorsal. The neck is narrow and varies in length.

The proglottides are well marked, and measure from 10 to 20 mm. in width. The breadth is greater than the length. There are numerous testes situated between the vitelline gland and the excretory canal at each side. From each testis fine seminal tubules are given off, which unite into a common duct to form the vas deferens, and end in the cirrus at the genital pore, which is situated near the anterior border of the segment in the median line. A vesicula seminalis is present.

The vaginal or female orifice is situated behind the male opening in the genital pore, and is continuous with the vagina, which leads into the receptaculum seminis. The ovaries are two in number, one at each side of the median line, and situated at the lower part of the segment. From each ovary a duct is given off that unites to form the common oviduct. In its course the oviduct receives the egg from the ovaries and the vitelline



FIG. 142.—Dibothriocephalus latus. Chain of segments, natural size. (*After R. Blanchard in Brumpt.*)

duct from the yolk gland. That portion in which the oviduct receives the vitelline duct and the secretion from the shell gland, and which marks the beginning of the uterus, is called the oötype (Fig. 137).

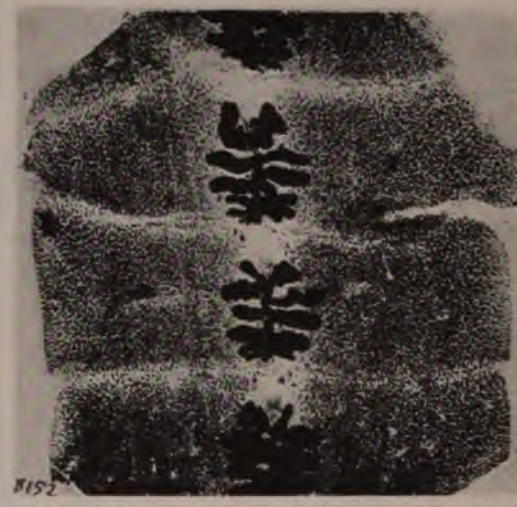


FIG. 143.—Ripe segments of Dibothriocephalus latus.



FIG. 144.—Ovum of Dibothriocephalus latus from the feces showing the operculum, *op*, at one pole (greatly magnified).

The oötype is continuous with the uterus, which, after coiling and forming a roset having from four to six convolutions, ends in the *metraterm* or uterine orifice, which is a separate aperture in the genital pore situated behind the male and female openings.

The genital pore in Dibothriocephalus is therefore, double, and

contains three orifices: One anterior—the larger—into which it opens, the cirrus and vagina, and one small one situated posteriorly for the opening of the uterus. The reproductive organs in Dibothriocephalus, therefore, resemble those in trematodes, except for the presence of a vaginal orifice in cestodes, which in trematodes is represented by a blind tube—Laurer's canal. The egg of Dibothriocephalus, like the egg of most trematodes, is operculated, measures about 70 by 45μ, and gives rise to a ciliated larva (Plate VIII).

Habitat.—Dibothriocephalus latus occurs in the intestine of man, dogs, and cats. It has been known to occur in Europe, especially in Switzerland, France, and northern Germany. It is also found in Asia, North America, Africa, and Madagascar.

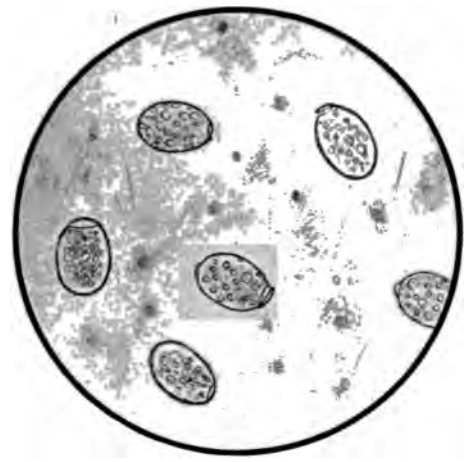


FIG. 145.—Ova of Dibothriocephalus latus in the feces. (Low power of the microscope.

Life History.—The eggs remain undeveloped for a long time in nature, but at a temperature of from 30° to 35° C. the ciliated onchosphere is formed in from ten to fifteen days (Schauinsland). When set free the onchosphere swims about in water for some time, and probably enters an unknown host (a mollusk) which transmits it to fish, such as salmon, pike, trout, etc., in the muscle of which it develops into a plerocercoid. When the fish are eaten, the plerocercoid develops into a tape-worm, and in about three or four weeks the eggs appear in the feces (Plate VIII).

Mechanism of Transmission.—The infective stage of *Dibothriocephalus latus*, as previously stated, is the plerocercoid found in the muscle and organs of the fish, and the parasite is transmitted to man by eating improperly cooked or raw fish. As the plerocercoid may likewise be found in the ovaries mingled with the eggs of the fish, it may also be transmitted by eating caviar. The prophylaxis consists in

the proper cooking of fish. The parasite may also develop in the intestines of dogs and cats, but it is much smaller in these animals than when found in the intestine of man.

The plerocercoid has been found in a variety of fishes, such as *Esox lucius* (pike), *Lota vulgaris* (miller's-thumb), *Perca fluviatilis* (perch), *Salmo umbla* (salmon), *Trutta vulgaris*, *T. lacustis* (trout), etc.

Diagnosis.—The presence of the adult tape-worm in the intestine is the source of gastro-intestinal disturbances and constitutional symptoms due probably to the absorption of toxic substances elaborated by the parasite. The chief symptoms are eosinophilia, a severe form of anemia, not uncommonly pernicious in type, and irregular fever. These symptoms may, however, all be produced by other causes, and a positive diagnosis must be based on the finding of proglottides in the feces, these being passed with fair regularity with the movements, or the detection of eggs, which are usually abundant and constant in the excrement.

The segments are easily recognized; they are flat and thin, much wider than long, whitish or yellowish in color, and having a brown or darkish spot (the uterus) in the median line. The eggs are large and oval, measuring about 70μ by 45μ, and operculated.

Pathogenesis.—The parasite produces a morbid condition called bothriocephalosis, characterized by severe anemia, irregular fever, and gastro-intestinal disturbances.

2. **Dibothriocephalus cordatus** (Leuckart, 1862).—The distinctive features of this parasite are the heart-shaped head, the absence of a neck, and the relatively small size of the adult worm, which measures only about a meter in length, and has from 400 to 600 proglottides. The mature segments are nearly square (5 to 6 mm. on both sides). The eggs are operculated, and measure from 75 to 80μ by 50μ. Evolution not known. It is a parasite of dogs and seals, and has been found only once in man.

3. **Dibothriocephalus parvus** (Stephens, 1908).—The scolex is unknown. The parasite was found in man in Australia by Elkington in the shape of three chains of segments passed by the rectum. The proglottides measure 5 by 3 mm., and are somewhat thicker than *B. latus*. The eggs are operculated, and measure about 60μ by 40μ. Lime cells were not found.

4. **Diplogonoporus grandis** (R. Blanchard, 1894).—This tape-worm is a common parasite of cetacea, and has been observed twice in man in Japan. The parasite is about 10 meters in length by 25 mm. in width. The scolex is unknown. The mature proglottides narrow anteriorly, measuring 1.5 mm. in width in front and 2.5 mm. behind and about 0.5 mm. in length. The genital pore are double in each segment and situated at each side of the median line. The whole

is comparable to a double tape-worm united laterally, but as the cephalic end is single in other species (*D. brauni*), the possibility of a monstrosity is out of the question. The eggs are operculated, and measure 63μ by 50μ. The evolution is unknown.



FIG. 146.—Diplogonophorus branni, natural size. (*After Leon in Brumpt.*)

5. **Diplogonoporus brauni** (Leon, 1907). This tape-worm has been found twice in man in association with (*Dibothriocephalus latus*) in Rumania. It is about 29 cm. in length; the head is pedunculated and the neck is absent. The proglottides are short and relatively broad (6 mm.). As the terminal segments are so atrophied that the posterior end appears very thin, it may readily be mistaken by the naked eye for the head and neck (Fig. 146).

6. **Sparganum mansoni** (Cobbold, 1883). This parasite was found at autopsy by Manson in the subperitoneum, near the kidney, and in the pleural cavity of a Chinaman. It was found by Scheube in the urethra of a Japanese. It is a slender, ribbon-like larva, whitish in color, and measuring from 8 to 36 mm. in length by 3 to 12 mm. in width. The adult worm is unknown.

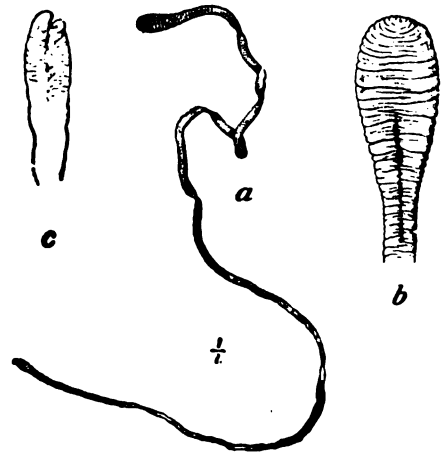


FIG. 147.—Sparganum mansoni. *a*, Natural size; *b*, cephalic end; *c*, caudal end. (*After Sambon in Brumpt.*)

7. **Sparganum prolifer** (Ijima, 1915).—This parasite has been found in man in Japan by Ijima, and in Florida by Stiles, encysted in the subcutaneous tissue. It measures 1 to 12 mm. in length by 2.5

mm. in breadth. This cestode has the peculiarity that it can multiply by transverse division and give rise to supernumerary heads, which detach themselves and fall inside of the cyst. The adult parasite is unknown.

Another dibothriocephalus larva, *Sparganum baxteri*, has been found by Baxter in an abscess of the thigh.

8. **Braunia jassyensis** (Leon, 1908).—This parasite has been found only once in man in Rumania. It measured 18 cm. in length by 12 mm. in width. External segmentation was poorly marked. The head was triangular in shape and the neck was indistinct. The parasite may be differentiated from *Ligula* by the ramification of the ovary and the disposition of the testes, which occupy almost the entire segment.

9. **Tenia solium** (Linnæus, 1767).—This cestode (Plate I) commonly known as the "pork tape-worm," is a common parasite, in the adult stage, of the intestine of man. Generally only one worm is found, but in a few instances two or more parasites have been reported as occurring simultaneously in the same patient.

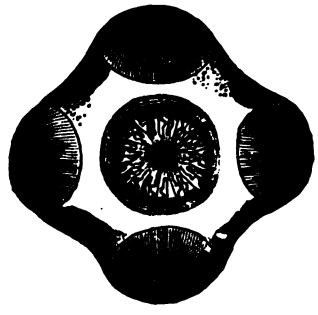


FIG. 148.—Tenia solium head. (*After R. Blanchard in Brumpt.*)

The length of the adult varies from two to eight meters, and is made up of from a few hundred to a thousand proglottides. The *head* is globular, slightly quadrangular, and measures about 1 mm. in diameter. It is provided with four suckers and a rostellum at the center, containing two rows of hooks, numbering about 25 to 50, and measuring 110 to 180μ. The *neck* is very short and slender. The mature segments are quadrangular in shape, and measure 10 to 12 by 5 to 6 mm., and are discharged passively with the feces in short chains. They are recognized by the character of the uterus, which is arborescent, and contains 7 to 10 branches on each side. The genital pores are single and alternate regularly on the outer edge of the segments. The eggs are almost spheric, measuring 31 to 38μ in diameter.

Habitat.—The adult worm lives in the small intestine of man and in the larval stage resides in the muscle of the pig. *Tenia solium* is as cosmopolitan as is the hog, that serves as its intermediate host. It is rare in the United States, but is found in Central and South America and in Europe.

Life History.—The hog is the normal intermediate host of *Tenia solium*. The eggs, or even segments or chains of segments of the parasite, may be swallowed by this animal. Man, monkeys, goats,

etc., may serve as intermediate hosts, but this is rare. On entering the intestine of the hog, the shell, or embryophore of the egg, is digested and the onchosphere is set free. With the aid of hooks it penetrates the mucous membrane of the intestines and reaches the lymphatics, the blood-stream, and the heart, and is finally carried by the blood to the subcutaneous tissue, muscles, and internal organs. In the new environment the embryo undergoes metamorphosis and encystment. It now begins to grow rapidly, and in about three or four months the bladder-worm larval stage is reached.

This larval stage which is called *Cysticercus cellulosa* (Fig. 149), and occurs in the muscles, liver, etc., appears as a white vesicle about 15 mm. in length by 7 to 8 mm. in width, but when under the skin may be spheric or irregular in shape (*Cysticercus racemosus*), when in the brain. The cysticercus consists of a scolex provided with four suckers and hooks invaginated into the cysts or bladder. It is probable that in this stage the larvæ may remain alive for many years. The name of "measly pork" is commonly applied to such infested flesh.



FIG. 149.—Cysticercus cellulosa in the muscles of a hog.

Mechanism of Transmission.—Man is infected by eating improperly cooked pork containing the cysticercus. (For further details see previous chapters.)

Pathogenesis.—In man the presence of the adult worm is the source of gastro-intestinal and hepatic disturbances, not uncommonly associated with colicky pains and diarrhea alternating with constipation. Emaciation and reflex nerve symptoms may also occur. Since man may act as an intermediate host, there is a probability of the entrance of the onchosphere into the system and the development of cysticercus in the organs, but this is a very rare occurrence.

Diagnosis.—Since, as stated in the previous chapter, the presence of *Tenia solium* in the intestine may or may not be accompanied by the symptoms enumerated, the diagnosis is based chiefly upon the finding of the egg or the segments or both in the feces. It should be remembered, however, that as the parasite has no birth pore and the eggs are retained in the uterus for some time, they may not be found in the feces in the early stage of the infestation.

Treatment and Prophylaxis.—There is no specific for the treatment of Teniæ. The drugs usually recommended are extract of male-fern,

given in capsules containing 4 to 12 minims each, or in the form of an emulsion on an empty stomach, followed, four to six hours later, by a saline purgative. Thymol, in doses of 40 to 60 grains, administered in divided doses of 10 grains each every half-hour, has given good results in some cases.

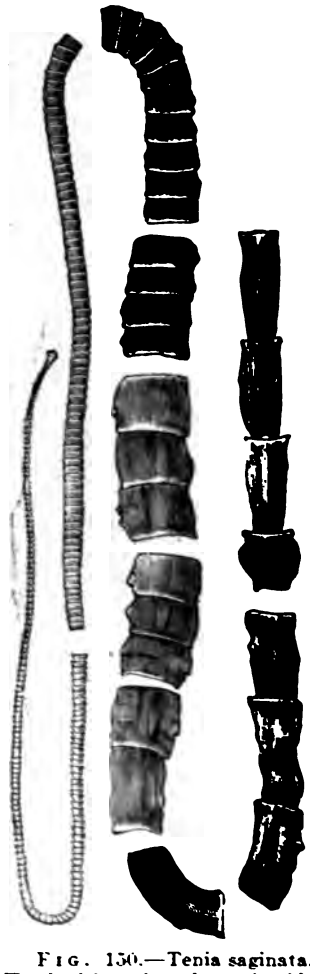


FIG. 150.—Tenia saginata. Head with series of proglottids taken from various regions of the strobila. (*After Leuckart in Hertwig.*)

The patient should be careful to keep his hands clean and to avoid infecting himself and others. The feces should be thoroughly disinfected or if possible, burned.

10. **Tenia saginata** (Goeze, 1782).—*Tenia saginata* (Fig. 150), commonly known as the beef tape-worm, like *Tenia solium*, is found in the small intestine of man. The parasite has a cosmopolitan distribution. The adult is found only in man and the cysticercus in cattle, although it has been produced experimentally in a number of animals. It is more frequent than *Tenia solium*, and is especially common in the tropics.

The scolex is pyriform or globular, and somewhat quadrangular, in shape, and provided with four rounded suckers and a pit in the center in place of the rostellum, which is absent. The neck is relatively long. The length of the adult worm is from 4 to 10 meters, and may contain as many as 1000 or more segments. The length of the mature proglottides is about twice the width, measuring 16 to 20 mm. long by 5 to 7 mm. wide.

The genital pore is single, situated at the side, and irregularly alternating. The proglottides are recognized by the arrangement of the uterus, which is arborescent in shape, and contains numerous branches—about 20 to 30 or more at each side. The old terminal segments are atrophied and shaped like a cucumber seed, hence the name, *T. cucurbitum*, also given to the parasite. Unlike *T. solium*, the segments of *T. saginata* escape from the anus by their own activity, and as found in the feces, appear usually singly or in pairs. Not uncommonly they may escape during the night, and are found by the patient on the bed covering in the morning. This ex-

plains why the patient becomes aware of their presence much earlier than is the case with *T. solium*. The eggs resemble the eggs of *T. solium*, from which they may be distinguished by being somewhat larger and oval in shape. They measure 30 to 40μ by 20 to 30μ.

Habitat.—The adult tape-worm is found in the intestine of man, usually attached to the upper part of the small intestine. The cysticercus is found normally only in cattle, but can be produced experimentally in other animals. Like *T. solium*, the number of parasites found is usually one or two, but several may be present in the same individual.

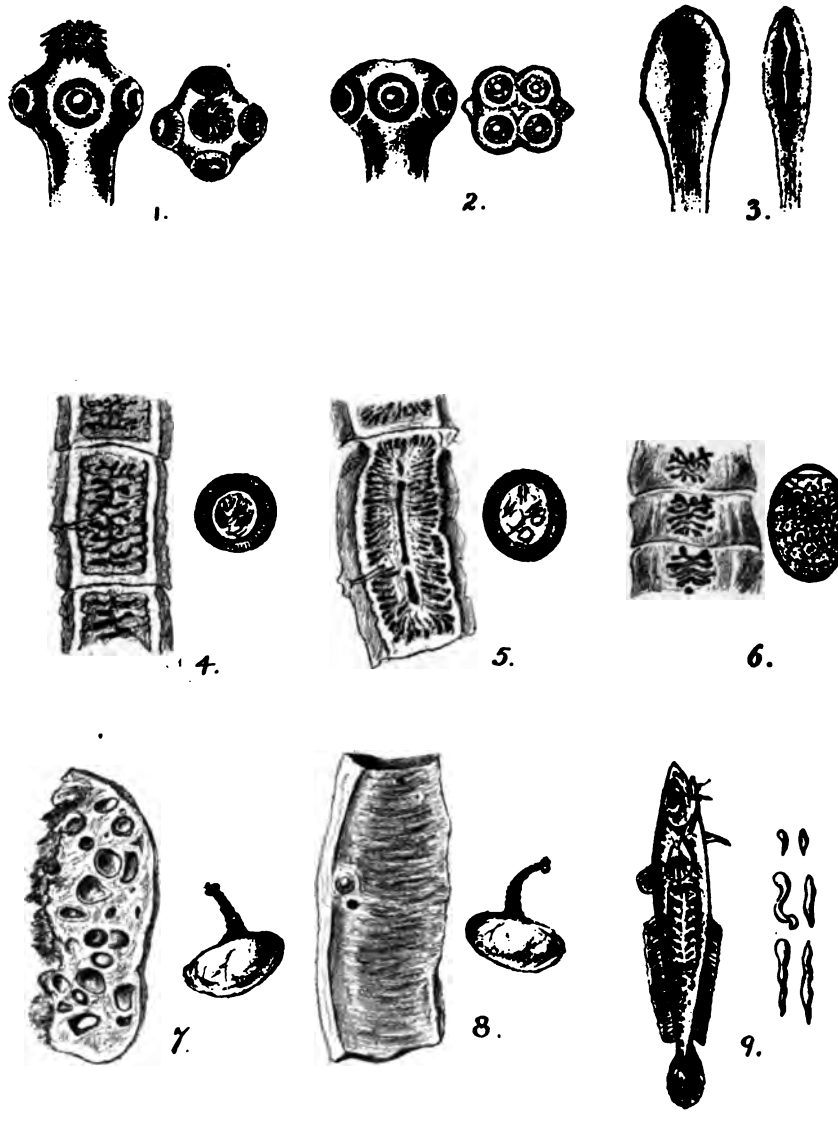
Life History.—Beef is the intermediate host. The eggs, as discharged with the feces or as found in the mature segments, contain a fully formed larva—onchosphere—which, on reaching the soil, is swallowed by cattle with contaminated food or water. The capsule is dissolved in the stomach, the onchosphere is set free, and on entering the intestine it penetrates the intestinal wall and reaches the lymphatics and the blood-stream. From the heart the larvæ are distributed through the circulation to different portions of the body, and become lodged in the muscles, where they undergo metamorphosis, becomes encysted, and, like *T. solium*, give rise to a cysticercus, *Cysticercus bovis* (Fig. 151).



Fig. 151.—Cysticercus bovis in the heart muscles of a cow.

The *Cysticercus bovis* is smaller than *C. cellulosa*, being only 7.5 to 9 mm. in length and about 5.5 mm. in breadth. It is found especially in the lingual, the masseter, and the pterygoid muscles. Man becomes infested by eating raw or improperly cooked meat containing the cysticercus. On reaching the stomach the cyst is digested and the scolex, being set free, attaches itself to the intestine, grows to maturity in about three months, and the cycle is repeated (Plate IX).

Mechanism of Infection.—As previously stated, man is infested by eating raw or improperly cooked beef containing the cysticercus. The infection is somewhat common. The small size of the cysts, their peculiar localization, and their limited number make their detection difficult, thus explaining the more frequent occurrence of *T. saginata* than of *T. solium*. As cattle, as a rule, are infested with the onchosphere of *T. saginata* through the medium of contaminated water or food, the infection is usually restricted, but conversely, the fact that pigs are coprophagous in habit results in the ingestion, by this animal, of entire segments or fragments of a chain of *T. solium* containing



Tenia Solium Tenia Saginata Dibothriocephalos Latus

PLATE IX-A.—Diagram illustrating the differential characteristics between—Tenia Solium—Tenia Saginata—and Dibothriocephalos Latus. 1. 2. 3. Heads—4. 5. 6. Segments and eggs—7. 8. Cysticercus in muscle and scolecis (bladder worm)—9. Plerocercoid in fish muscle and free.

thousands of eggs. As a consequence, the infection is usually quite marked and generalized, and as the *Cysticercus cellulosa* is relatively larger and easier of recognition than *Cysticercus bovis*, its detection is rendered simpler, and the use of such infected meat is readily avoided.

Pathogenesis.—*T. saginata* is said to produce a more severe anemia than *T. solium*, and the expulsion of the adult parasite is also said to be more difficult.

Diagnosis.—The presence of the adult tape-worm does not necessarily imply the occurrence of any appreciable symptoms in the patient, and the diagnosis is, therefore, based on the finding of segments or eggs or both in the feces. Not uncommonly the patient's attention is first attracted to the condition by the finding of segments on the bed linen, they having been passed during the night. Unlike the segments of *T. solium*, the segments of *T. saginata* force their way through the rectum by their own activities, and as this may occur at any time, and more especially during the night, in suspected cases the attention of the patient should be directed to this possible occurrence.

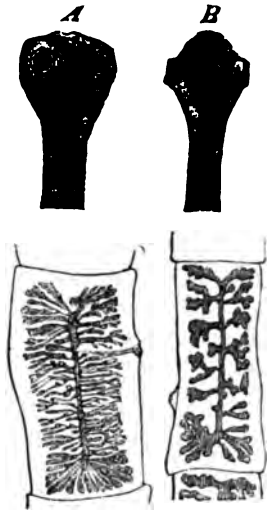


FIG. 152.—Head and ripe segment of Tenia saginata, *A*, and Tenia solium, *C*. (*After Hertwig.*)

The proglottides of *T. saginata* are somewhat shorter than are those of *T. solium*. The cucumber shape of the terminal segments in *T. saginata* is characteristic, as is also the shape of the uterus, which ramifies freely and contains from 20 to 35 branches on each side. Examination of the segments is accomplished by pressing the specimen between two slides and examining them with a magnifying glass or under the low power of the microscope. The previous addition of strong acetic acid solution or a 10 per cent. sodium hydroxid solution clarifies the segment and renders the branches of the uterus more prominent. Malformation of the proglottides is not uncommon.

Treatment and Prophylaxis.—The medicinal treatment is the same as for *T. solium*. The prophylaxis consists in preventing the human feces from contaminating the food of cattle, and inspecting the meat, specially the tongue and the pterygoid muscles, together with the muscles of mastication, in the abattoir.

DIFFERENTIAL CHARACTERISTICS OF TENIA SOLIUM AND TENIA SAGINATA

	T. Solium	T. Saginata
Head	Globular, size about 1 mm. in diameter. Rostellum with two rows of hooks.	Quadrangular, 1.5 to 2 mm. in diameter. Rostellum and hooks absent.
Length of adult tape-worm	From 2 to 8 meters.	From 4 to 10 meters.
Number of segments	From 700 to 1000.	About 1000 or more.
Size of mature proglottides	From 10 to 12 mm. in length by 5 to 6 mm. in width.	From 16 to 20 mm. in length by about 4 to 5 mm. in width.
Uterus	Ramified, 7 to 10 branches.	Ramified, 20 to 35 branches.
The cysticercus stage	*Cysticercus cellulosæ* found in pork, usually in large numbers, and easily recognized; hence the rarity of infestation in man.	*Cysticercus bovis* found in cattle usually in small numbers, and detected with difficulty; hence the frequency in man.
Eggs	Almost spheric, 31 to 38μ in diameter.	Somewhat oval—20 to 30 by 30 to 40μ.

Tenia echinococcus (von Siebold, 1853).—The most characteristic feature of the cyst produced by *T. echinococcus* is that it gives rise to hundreds or even thousands or millions of scolices, which develop from a single onchosphere, whereas other Teniæ produce one scolex, or at most only a few. This peculiarity, it seems, has led Castellani and Chalmers (Manual of Tropical Medicine, 1910) to place this parasite in a separate genus, *Echinococcus*.

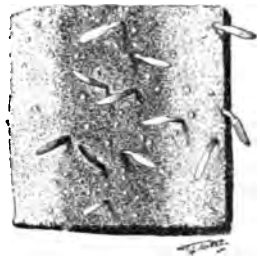


FIG. 153.—Tenia echinococcus (*Echinococcus granulosus*) attached to the mucosa of the intestine of a dog. Experimental infestment. (*After Brumpt.*)

Echinococcus (Rudolphi, 1802).—The echinococci are small tape-worms, commonly found in the adult stage in the intestines of dogs, wolves, and jackals, and in the cysticercus stage in the internal organs of man, sheep, oxen, and pigs, in the form of peculiar cyst-like tumors, that vary in size and in number, and are known as *hydatid cysts*. The presence of these cysts in man gives rise to the peculiar morbid changes to which the name "hydatid disease" has been given.

Hydatid disease was probably known in Hippocrates' day. Redi, in 1684, suggested the animal nature of these cysts, and Zeder, in 1800, placed them in a separate group—*cystici*. Previous to this, in 1760,

Pallas showed their relationship to tape-worms (*Tenia hydatigena*). Küchenmeister, in 1851, demonstrated by feeding experiments that they were only the larvæ of tape-worms, and that, to complete their life history, two hosts were required.

For many years, and even up to the present time, hydatid disease has been regarded as due to but one variety of parasite, and though it appears doubtful whether there are two, the character of the cyst and the geographic distribution of the disease tend to divide the genus into two species, namely: *Echinococcus granulosus* or *T. echinococcus unilocularis*, and *Echinococcus multilocularis* or *T. echinococcus multilocularis*.

11. **Echinococcus granulosus** (Batsch, 1789).—This echinococcus also called *Tenia echinococcus unilocularis* (Fig. 132) (Zeder, 1803; von Siebold, 1853), is a very small cestode, found in the intestine of the dog, wolf and jackal. The adult parasite is club or bottle shaped, and is made up of a head, neck, and three or four segments (the scolex and three proglottides). It measures only 2.5 to 5 or 6 mm. in length by about 0.5 mm. in width at the posterior third, which corresponds to about the middle of the posterior segment.

The scolex is provided with four suckers and a rostellum with two rows of hooks, from 28 to 50 in number, varying in length from 30 to 45μ. The genital pores alternate. Numerous testes are present. The uterus displays only lateral diverticula, but no true branches, and contains from 400 to 800 eggs. The eggs are globular (somewhat resembling the eggs of *T. solium*), and from 30 to 36μ in diameter.

Habitat.—The adult parasite is found in the small intestines of dogs, jackals, and wolves, usually in large number, and attached between the villi of the intestine. The parasite in the bladder-worm stage is found in man, commonly in the liver, lungs, or spleen, etc. It has been found also in monkeys, dogs, cats, bears, sheep, goats, cattle, camels, rabbits, zebras, horses, etc.

Life History.—The life history of *E. granulosus*, previously stated, does not differ essentially from the life history of *T. solium* or *T. saginata* (Plate IX), except that while each onchosphere of the two last named worms gives rise to a single cyst and scolex, *E. granulosus* has greater vegetative reproductive powers and is capable of producing a great number of scolices in the same cyst from a single onchosphere. The course of the cycle may be summarized as follows:

The dog is the primary host, and man is the secondary host of the parasite. Man is infected with the egg or onchosphere discharged by the dog with the feces, either directly by contact with an infected dog or indirectly through the medium of contaminated food, water, etc.

The dog is infected by swallowing the cysts, which as previously stated, may be found also in the organs of several wild and domestic

animals. On reaching the stomach the cyst is digested, the scolex is set free, attaches itself to the mucosa of the intestine, grows to adult size, and the cycle is repeated. (For further details see previous chapter.)

Mechanism of Transmission.—The infective stage of the parasite for man is the egg or onchosphere, as found in the feces of dogs and other animals, and man may become infected either directly through



Fig. 154.—Hydatid cysts in the liver of man.

contact with the infected dog or indirectly through the ingestion of contaminated food, water, etc.

Pathogenesis.—The presence of the parasite in man is the cause of a morbid condition known as *hydatid disease.* As the cyst grows slowly, the organ may adapt itself to the pressure and give rise to only very slight disturbances. A rupture of the cyst and escape of the fluid are followed by toxic symptoms, urticarial eruptions, rigors, etc. Pressure on vital organs, such as the brain, may be the cause of acute

and grave symptoms. Hepatic, pulmonary, cardiac, and renal disturbances may occur, according to the location of the cyst.

Diagnosis.—The diagnosis of hydatid disease is always made with difficulty, especially at the beginning and even late in the course of the infection. Specific symptoms, upon which a diagnosis can be made with certainty, are not present. The most important points that should be considered in making the diagnosis may be summarized as follows:

Symptoms.—The presence of a tumor, with or without hydatid fremitus, a certain degree of eosinophilia, and a history of occasional attacks of urticaria, if other parasitic infections can be excluded, are important points in the diagnosis.

The X-rays.—The *x*-rays may give valuable information and aid in the diagnosis and also serve as a guide in the operative treatment of the disease.



FIG. 155.—Hydatid cysts in liver of camel (*Camelus bactrianus*).

Exploratory Puncture.—The exploratory puncture of the tumor, a method formerly employed extensively, is not recommended at the present time, and this procedure, as a rule, is contraindicated, for not uncommonly, even when made under aseptic precautions, it may give rise to secondary infection and suppuration, due to the introduction into the cyst of *B. coli*, which is not uncommonly present in the bile-ducts. An extravasation of the fluid is commonly the source of irritation, urticaria, etc., and, besides the escape of scolices into the surrounding tissue or into the peritoneum may give rise to secondary cyst formation.

Serodiagnosis.—This is based on the fact that the presence of a hydatid cyst gives rise to the development of specific antibodies, whose presence can be determined either by the precipitin or the complement-fixation test.

Precipitin Reaction.—As previously stated in an earlier chapter, equal parts of the patient's serum and hydatid fluid, obtained from another case, are mixed. If a distinct flocculent precipitate is produced within from five to thirty minutes the test may be said to be positive. The duration of the test should not exceed one hour, and

if after this time the mixture remains clear or only a slight cloudiness or fine precipitation occurs, the test may be regarded as negative. In performing the test the serum of a normal person and that of a case of known hydatid disease should also be tested as negative and positive controls respectively.

Complement-fixation Test.—The complement-fixation test, as previously stated, is applied in a similar way to the Wassermann reaction for syphilis, using the fluid of a hydatid cyst as antigen.

The antigenic dose or "unit" of the liquid of the hydatid cyst from another case is first determined by titration, and *this should be about one-half or less of the anticomplementary dose.* The unit of antigen is the smallest amount of antigen which, in the presence of 0.1 c.c. positive serum (hydatid disease) and one unit of complement (0.5 c.c. of a 10 per cent. dilution of guinea-pig normal serum), when incubated for forty-five minutes at 39° to 40° C., absorbs or neutralizes the units of complement, as shown by the fact that if, after incubation, sheep hemolytic amboceptors (one unit) and sheep erythrocytes (1 c.c. of a mixture of 2.5 per cent. washed erythrocytes suspended in salt solution) are added to the mixture and incubated again, no hemolysis takes place. The same unit of antigen, however, under the same conditions, in the presence of normal serum, should not induce absorption of the complement, as shown by the fact that hemolysis is complete when sheep amboceptors and sheep erythrocytes are added to the mixture after the first incubation.

For the complement-fixation test, therefore, the following substances are required:

1. Antigen: Fluid of a hydatid cyst.
2. Complement: Guinea-pig normal serum.
3. Serum of patient to be tested, previously inactivated by being heated to 54° C. for thirty minutes, to destroy the complement.
4. Sheep amboceptors.
5. A 2.5 per cent. mixture of defibrinated sheep erythrocytes, free from serum, and suspended in physiologic salt solution.

The Test.—To two tubes, A and B, are added 0.1 c.c. of the patient's serum (inactivated) and 0.05 c.c. of normal guinea-pig serum (0.5 of a 10 per cent. or 1 c.c. of a 20 per cent. dilution in salt solution). To tube B, in addition, one unit of antigen (hydatid fluid) is added. The tubes are shaken and incubated at 39° to 40° C. for forty-five minutes in a water-bath, during which time the tubes are again shaken about every fifteen minutes.

After incubation the hemolytic serum is added to each tube, namely, sheep amboceptors (about 1.5 to 2 units) and 1 c.c. of the sheep erythrocytes suspension. Salt solution is added to each tube to equal volume, and after shaking, the mixture is again incubated at

39° to 40° C. for from thirty to sixty minutes. If, after the second incubation, both tubes are hemolyzed, the reaction is negative, whereas if tube A is hemolyzed and tube B is not, the reaction is positive.

In making the test, a known positive and a known normal human serum should also be tested as control. (For further details on complement fixation see Chapter XXX.)

Treatment and Prophylaxis.—The medicinal treatment is purely symptomatic. Surgical treatment may consist either in the evacuation of the contents of the cyst or in the complete removal of the tumor. Mere evacuation of the contents of the cyst is dangerous and of doubtful efficacy. As a result the scolices may escape into the surrounding tissue or into the peritoneum or pleura, etc., and give rise to secondary growth. Complete removal of the cyst by encapsulation is the procedure of choice, care being taken during the operation to avoid the escape of the contents of the cyst into the surrounding tissues.

As the echinococcus is transmitted to man and domesticated animals by the dog, which harbors the adult parasite in the intestines and disseminates the eggs with the feces, exclusion of dogs from the house and avoidance of contact with this animal are recommended. In practice, however, it is almost impossible to modify the relation that exists between man and dogs. On the contrary, rigid inspection of the slaughter-houses; the incineration of all meat infested with hydatid cysts, and the education of the laity and dealers in meat in general as to the danger of feeding dogs with such meat, uncooked, will accomplish better results and with less difficulty.

A very important prophylactic measure and one usually neglected, is the examination of the house dog for the presence of echinococcus eggs or of the adult parasite in the feces and immediate removal and proper treatment of the infected animal.

12. **Echinococcus multilocularis** (Leuckart, 1863).—This parasite in the adult stage probably lives in the intestine of the dog and in the larval stage inhabits man, in whom its presence gives rise to ulcerative hydatid cyst, neoplastic in nature, and known as *alveolar* or *multilocular hydatid cysts*.

History.—The disease was first described by Ruysch in 1721 as a colloidal cancer. Virchow, in 1856, demonstrated the parasitic nature of the growth. By feeding experiments Mangold and Müller claimed to have obtained from the scolex in the cyst a *Tenia* which was different from *E. granulosus* in the number of hooks and the distribution of the eggs. Further, Mangold asserts that he succeeded in reproducing multilocular cysts in a young pig by feeding the animal with the adult *Teniæ*. Stiles, Sterling, Verco, and others regard this parasite as different from *E. granulosus*.

Individuality of the Parasites.—It is generally admitted that the slight morphologic variation in the adult *Tenia*, such as the shape and number of hooks and the distribution of the eggs in the uterus, is not a sufficiently important point of differentiation. The chief difference lies in the character of the cyst produced by the larva and the geographic distribution of the disease. Thus, *E. multilocularis* is more common in South Germany, Switzerland, the Austrian Alpine region, and Russia, and is absent in Iceland and Australia. It is also said to be common in the north of South America, where *E. granulosus* is usually absent.

From what has been said it may be seen that the differentiation between the two parasites is based chiefly upon the cyst produced by the larva, which is multilocular or alveolar in character, and neoplastic in nature. It is possible that this difference in the character of the cyst does not depend so much upon the parasite *per se* as upon environmental conditions furnished by the tissue of the host. It is probable, for instance, that the individual condition of the parasitized organ, together with the specialized proliferative nature common to the larval stage of the parasite (*E. granulosus*), prevents the encapsulation of the cyst, with the result that infiltration readily takes place and metastasis may occur, thus giving rise to the multilocular character and neoplastic nature of the growth. This being the case, the two parasites, *E. granulosus* and *E. multilocularis*, may, therefore, properly be regarded for the time being, as identical until further evidence is adduced to the contrary.

Life History.—The evolution is identical with that described for *E. granulosus*, with this difference: that the onchosphere, on being lodged in the tissues and undergoing metamorphosis into the ameboid form, begins to grow as such vegetatively without encystment, with the result that it gives rise to plasmodial masses that gradually, by prolongations, infiltrate the surrounding tissue. In time these germinative prolongations become separated from the original growth, forming numerous and independent "parasitic plasmodia" or ameboid embryos (Melnikoff).

During the growth disintegration may take place in the center of the cyst, and metastasis of the growth may also occur. (For further details see the previous chapter.)

Mechanism of Transmission.—The mechanism of transmission, treatment, and prophylaxis is the same as for *E. granulosus*. Complete removal of the growth is more difficult and sometimes almost impossible.

Pathogenesis.—*Echinococcus multilocularis* may produce a primary growth in the liver, brain, spleen, kidney, etc., and metastasis to any part of the body may occur. The symptoms vary according to the

location of the tumor. After some time—perhaps years—anemia, weakness, emaciation, or secondary infection may cause the death of the patient.

13. **Hymenolepis nana** (von Siebold, 1852).—This parasite is the smallest tape-worm known to inhabit the intestine of man. It was found by Bilharz in 1855 in a child in Egypt. The adult measures 10 to 40 mm. in length by 0.5 to 0.9 mm. in width. The head is small (0.3 mm.), has four suckers, and is provided with a rostellum and

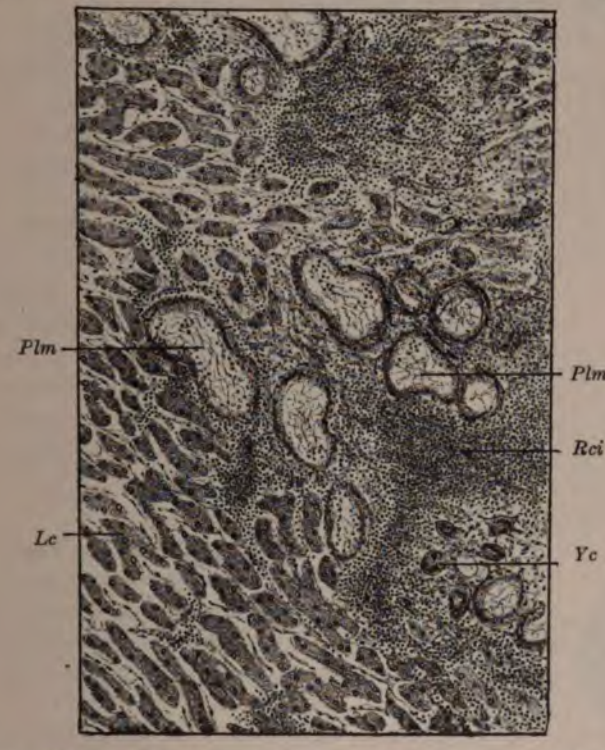


FIG. 156.—Echinococcus mutilocularis in the liver. *Plm*, plasmodial forms of the parasite; *Rci*, round cell infiltration; *Gc*, giant cells; *Lc*, liver cells. (*After Deve in Brumpt.*)

hooks (24 to 30 in number). The adult worm has about 150 very small proglottides, a mature segment measuring only 14 to 30μ in length by 0.4 to 0.9 mm. in width. The genital pore is marginal and on the same side. The mature uterus contains from 30 to 50 eggs, and is oval in shape, 35μ in length, and provided with a small knob at each pole.

Habitat.—This cestode is a common parasite of the rat, but it may also inhabit the lower part of the small intestine of man, in whom it is by no means rare. Of all cestodes, this may be said to be the most

common. Calandruccio found it in 10 per cent. of the children in Sicily, and Stiles encountered it in 4.8 per cent. of the children in Washington. It is a cosmopolitan cestode, common to Algeria, southern United States, the Philippine Islands, and Japan. The number of parasites varies from a few to several thousand in the same patient. Because of its small size, the parasite is apt to be overlooked, but as the segments are usually broken and disintegrated before they are discharged, the eggs may escape and may be found in the feces without difficulty.

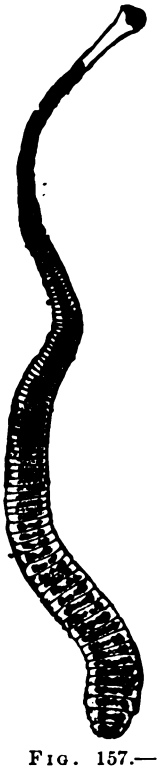


FIG. 157.—Hymenolepis nana. Enlarged × 12. (*After Leuckart in Brumpt.*)

Life History.—According to Johnston, Nicolle, and Minchin, the flea (*Ceratophyllus fasciatus* and *Xenopsylla cheopis*) serves as the intermediate host. The onchosphere develops into a cysticercoid in the body of this insect, which, when swallowed by the rat, develops into a tape-worm in the intestine. The experiments of Grassi have demonstrated the development of the cysticercus in the villi of the intestine. The rupture of the mucosa liberates the scolex, which attaches itself to the intestine and develops into an adult worm. The time occupied in complete evolution is about two weeks. It is probable that a similar evolution occurs in man, and this explains the possibility of the occurrence of an autoinfection, and also accounts for the large number of parasites not infrequently found in one individual.

Mechanism of Transmission.—Man is probably infected through eating food contaminated by infected rats. The infective stage in the life cycle of the parasite may be either the onchosphere, as found in the feces of rats, or the cysticercoid stage seen in the infected flea.

Pathogenesis.—When but few parasites are present, there may be no appreciable symptoms. The existence of a considerable number, however, may give rise to gastro-intestinal disturbance and possibly acute symptoms which are regarded toxic in origin, such as tetanic, epileptic, or eclamptic convulsions. The infection may not uncommonly spread to others living in crowded dwellings.

Diagnosis.—The diagnosis can usually be made without difficulty, as when carefully sought for the proglottides or eggs of the parasite are readily found in the feces.

Treatment and Prophylaxis.—Male-fern is the most reliable drug in the medicinal treatment. Thymol may also cause expulsion of the parasite. As a prophylactic measure, the eating of food contaminated

by rats should be avoided. The fact that this parasite is one of the few cestodes that requires no intermediate host to complete its life history renders auto-infestation possible, and suggests the transmission, to other individuals, either directly or indirectly, through the contamination of food with the onchosphere. The isolation of the

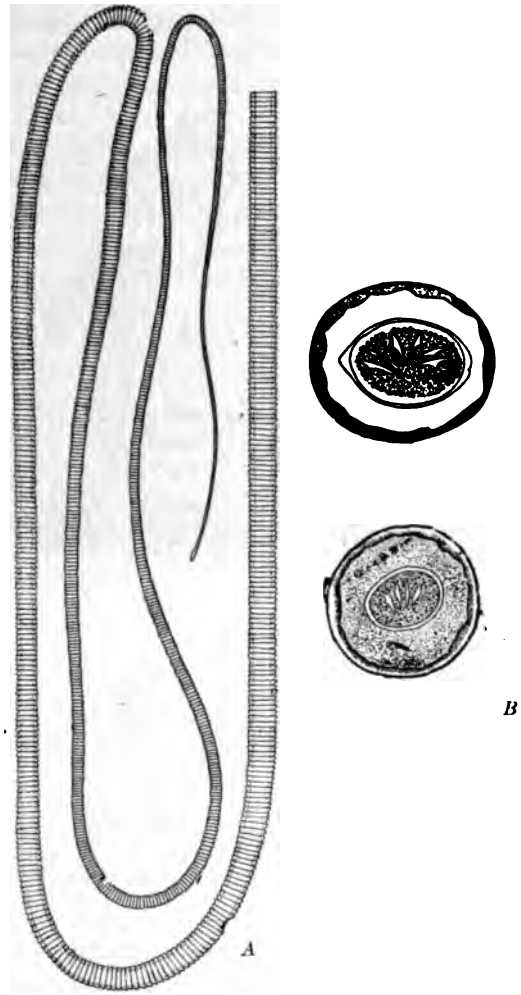


FIG. 158.—Hymenolepis diminuta. *A*, Adult, natural size. (*After Brumpt.*) *B*, eggs. (*After R. Blanchard in Brumpt.*)

patient, particularly of those living in crowded dwellings, therefore, becomes imperative. Similarly proper cleanliness should be enforced to prevent reinfection.

14. Hymenolepis diminuta (Rudolphi, 1819).—This cestode is a natural parasite of the rat (*Mus norvegicus; Mus rattus; M. alexandrinus,*

etc.). The adult parasite measures 20 to 60 cm. in length by about 3.5 mm. in width. The head is small, from 0.2 to 0.5 mm. in diameter, and is provided with four suckers and a rudimentary rostellum without hooks. The anterior segments show a yellow spot, caused by the distended receptaculum seminis, whereas the posterior segments show a dark brownish spot due to the matured uterus. The eggs are slightly oval, measuring 60 to 85μ in their longest diameter.

Habitat.—The parasite is commonly found in rats and occasionally in man, attached to the lower part of the small intestine.

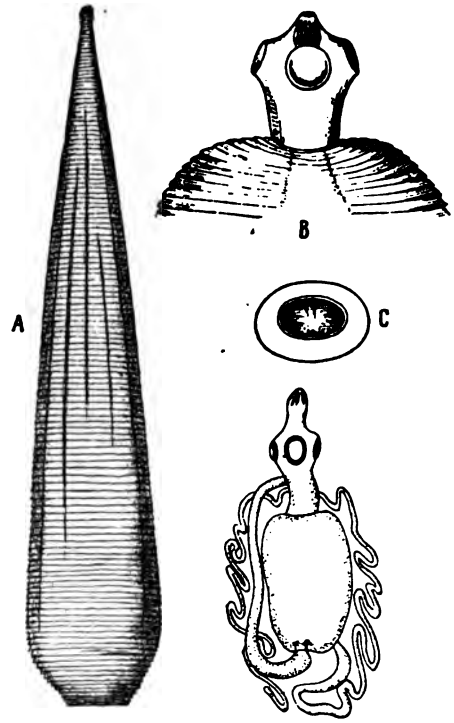


FIG. 159.—Hymenolepis lanceolata. *A*, natural size; *B*, head enlarged × 100; *C*, egg enlarged × 300; *D*, larval form. (*A, B and C after Railliet, and B after Daday in Brumpt.*)

Life History.—The cysticercus stage has been found in several insects: Lepidopteras (*Asopia farinalis, Anisolabis anulipes*), coleopteras (*Akis spinosa*), and in fleas (*Ceratophyllus fasciatus*). The experiments of Grassi and Rovelli have demonstrated that the adult tape-worm develops in the intestine of man and rats in about fifteen days after the cysticercus has been swallowed.

Mechanism of Transmission.—Man usually becomes infected through eating food contaminated by insects. The parasite most commonly occurs in infants and children.

15. **Hymenolepis lanceolata** (Blochmann, 1782).—This cestode is a common parasite of ducks, geese, and other fowl and birds. It has also been found in man. The adult worm is lanceolate in shape, and measures from 3 to 13 cm. in length by 5 to 18 mm. in width. The head is small and globular, and is provided with four suckers and a rostellum with hooks.

Life History.—The cysticercoid develops in a cyclops (*Diaptomus spinosus*), which, when swallowed by birds, develops into the tape-worm. Infection in man probably takes place through the imbibition of contaminated water.

16. **Davainea madagascariensis** (Davaine, 1869).—This cestode is common in children. The adult measures 25 to 30 cm. in length, 1.4 mm. as its maximum width, and is made up of from 500 to 700 proglottides. The scolex is about 1 mm. in diameter, and has about

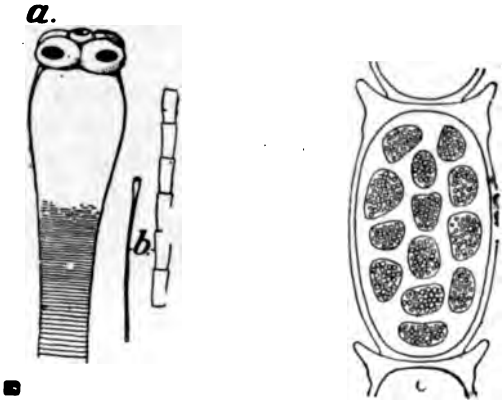


FIG. 160.—Davainea madagascariensis. *A*, head enlarged; *b*, cephalic end and segments, natural size; *c*, sagittal section of a segment showing the oviferous capsule. (*A and B after R. Blanchard and C after Linstow in Brumpt.*)

90 hooks. The genital pores are on one side and near the proximal end. The uterus consists of a number of tubes rolled on each side into a spheric coil. When mature, the uterus will uncoil and almost fill the entire proglottis; it finally ruptures, the eggs escape into the body, and, by proliferation of the parenchyma, a capsule is formed, known as the *egg capsule*. As many as from 300 to 400 of these capsules are found in a matured proglottis, and each contains many eggs. The eggs are small, slightly oval, and contain an onchosphere which measures 8 by 15μ without the shell.

Habitat.—This worm was first found in children by Grenet. According to Blanchard, up to 1899, 25 species of Davainea have been found among mammals and birds and several other species were described later. The parasite is commonly seen in rats, hares, and birds in general.

Life History.—The life history is not known. It has been suggested by Blanchard that the cysticercus develops in the cockroach (*Periplaneta orientalis* or *P. americana*).

17. **Davainea asiatica** (von Linstow, 1901).—The description of this worm is based upon a single specimen found by Auger, in Persia, in an adult. It measured 298 mm. in length by 1.17 mm. in width, and consisted of 750 immature proglottides without scolices. Genital pores are situated on the same side. The development of the eggs and the life history are not known.

18. **Dipylidium caninum** (Linnæus, 1758).—Dogs and cats are the normal hosts of this tapeworm, but it is not uncommonly found in man. Blanchard, in 1907, collected 60 cases, most of which occurred among young children. The adult worm measured 15 to 40 cm. in length and 1.5 to 3 mm. in breadth. The scolex is provided with four suckers and a well-developed rostellum containing three or four rings of hooks. The proglottides are elliptic in shape, somewhat

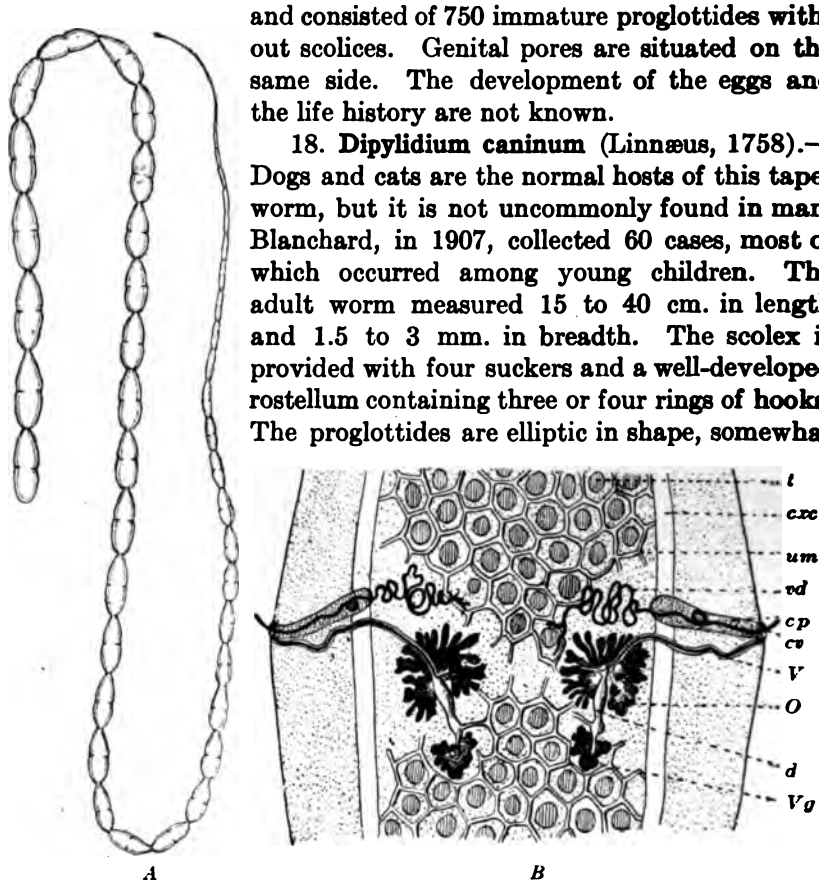


FIG. 161.—Dipylidium caninum. *A*, natural size; *B*, segment enlarged. *t*, Testes; *exc*, excretory canal; *um*, uterine matrix; *vd*, vas deferens; *cp*, cirrus pouch; *cr*, cirrus; *v*, vagina; *o*, ovary; *d*, dilatation (?); *vg*, vitelline gland. (*After Neuman in Brumpt.*)

resembling a cucumber seed in form, and when matured, they are much longer than broad. The genital pore is double—one on each side of each segment—and corresponds to the genital organs, which are also double. The eggs are round, and measure 43 to 50μ in diameter.

Life History—The cysticercoid may develop in the dog-louse (*Trichodectes canis*) and in that of the cat, as demonstrated by Melni-

kow in 1751, or in the flea (*Pulex irritans*). The common intermediate host, however, as demonstrated by Grassi and Rovelli, is the dog-flea (*Ctenocephalus canis*) or that of the cat. By their own activity the mature proglottides force their way through the anus and invade the fur or hair of the dog or cat, and the eggs are deposited here. On being swallowed by the flea these eggs liberate the onchosphere, which develops into a cysticercoid in the body of the insect. The dog swallows the flea and infects itself. In like manner the cat is infected by licking its fur. Man is infected by eating contaminated food. Dogs may transmit the cysticercoid to man.

OTHER PARASITIC CESTODES OF MAN

Tenia africana (von Linstow, 1900).—This parasite has been found twice in man in German East Africa. The adult worm measures about 1.4 meters in length. The scolex is provided with an apical sucker in place of a rostellum, in addition to the four ordinary suckers. The mature proglottides, which number about 600, measure about 9 mm. in width, and are always broader than they are long. The genital pores alternate irregularly on the lateral border. The testes are numerous; the vas deferens is convoluted, and the cirrus pouch is pear shaped. The ovaries are large and double, and the vitelline gland is single and situated at the posterior border. The uterus consists of a median portion and from 15 to 20 non-ramified lateral branches. A receptaculum seminis is present. The eggs are round or slightly oval.

Tenia philippina (Garrison, 1907).—This cestode was found by Hare in the Philippines in 1905. The worm measures 80 to 100 cm. in length, by about 1 cm. in breadth, and contains about 800 proglottides, each 0.8 to 1 mm. in length by 4 to 5 mm. in breadth. The vesicula seminalis is absent, and the cirrus pouch is present. Genital pores are irregularly alternate; there are two ovaries, and the uterus has numerous lateral dichotomous branches. Eggs are oval, 35 to 41μ by 26 to 35μ. The life history is unknown.

Tenia bremneri (Stephens, 1907).—This parasite was found by Bremner in northern Algeria and showed no head. The segments measured on an average 28.6 mm. by 8.5 mm. The uterus showed 22 or 24 ramified branches. The genital pore was situated on the side and behind the middle of the segment. The eggs were slightly oval (38 by 30.4μ). The life history is not known.

Tenia hominis (von Linstow, 1902).—This cestode was found by Anger in Siberia. The scolex is unarmed, but shows the presence of a ring-shaped swelling behind the suckers. The worm is 70 mm. in length.

Tenia confusa (?) (Ward, 1896).—This parasite has been found by Ward in Lincoln, Nebraska. The worm is 8.5 meters long by 5 mm. in width. Scolex unknown. The segments measure 27 to 35 mm. long by 3.5 to 5 mm. in breadth. The genital pore is irregularly alternate. Testes are numerous; ovaries are double; and the uterus has from 14 to 18 dichotomous branches. Eggs are oval (39 by 30μ). The life history is not known.

LABORATORY DIAGNOSIS OF CESTODES

Search for the Adult Parasite.—The material for examination is prepared as follows: The feces, when hard, are first softened and then suspended in an excess of a 4 per cent. formaldehyd solution. It is now filtered through a sieve the mesh of which is about 0.5 to 1 mm. A screen basket, or a double layer of gauze will answer the purpose. Any remaining clumps of feces are gently broken up and the sediment washed in running water for a few minutes. The residue is now spread on a black or dark colored tray containing sufficient water, and then examined by the aid of a magnifying glass. Any suspicious object is carefully removed to a slide and examined under the microscope for identification.

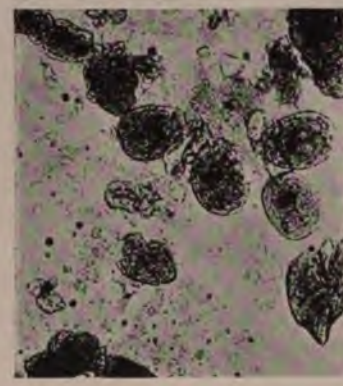


FIG. 162.—Material, including scolices, from hydatid cyst.

The proglottides of the cestodes are, as a rule, easily recognized, for they are relatively large and visible to the naked eye, but the small size of the segments of some species, such as *Hymenolepis nana*, *H. diminuta*, and a few others, renders their recognition somewhat difficult, because of the resemblance they bear to vegetable fibers and other detritus commonly found in the feces. It may also happen that these artefacts may be mistaken for proglottides or scolices; hence the necessity for making a careful examination, with the aid of a magnifying lens or the microscope, of the suspicious objects found in the feces.

The proglottides normally discharged with the feces are usually matured, and contain a large number of eggs. In doubtful cases, therefore, it is a safe procedure to tease the suspected material in a small quantity of water on a slide, and then make cover-glass preparations and search for the eggs with the aid of a microscope.

The identification of the head of a cestode should always be made with the aid of a magnifying lens or under the microscope, and the

diagnosis should be based upon the presence of suckers or of a sucker and rostellum, with or without hooks, as the case may be (Fig. 162).

Search for the Larval Stage.—The larval stages of cestodes in general are rarely seen in man. There are a few species, such as *Sparganum mansoni*, *S. prolijer*, *Hymenolepis nana*, and *Tenia solium*, the cysticercus stage of which has been reported in man, but these are only occasional findings and are practically unimportant. Contrary to this, the larval stage of *Echinococcus granulosus* (*T. echinococcus*) and that of *E. multilocularis* are quite common and of great importance in parasitology, since they are the cause of definite and grave affections in man and animals, and hence only these need be considered here.

The larval or bladder-worm stage of *Echinococcus granulosus* and *E. multilocularis* appears in man in the form of cysts that vary in size and are known as hydatid cysts. It most frequently affects the liver, but may also occasionally be found in the lungs and in other internal organs.

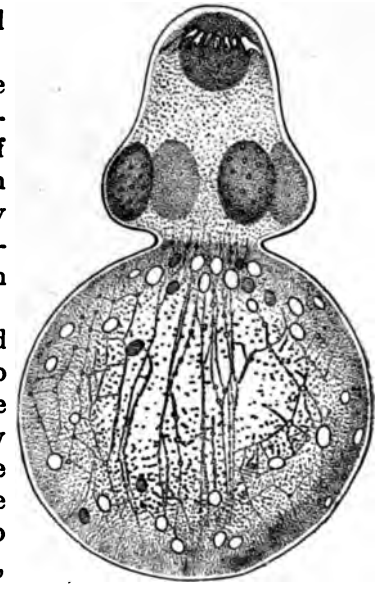


FIG. 163.—Vesicular transformation of a scolex after evagination of the head from the cyst. (× 350, *after Deve in Brumpt.*)

In making a diagnosis of hydatid cyst it was formerly customary to make an exploratory puncture of the cyst, but this procedure, as previously stated, is now contraindicated because of the possibility of the escape of the contents of the cyst (the scolex) into the surrounding tissues or serous sac, and the danger of giving rise to secondary cyst formation. Spontaneous rupture of the cyst, however, may occur and its contents be discharged externally, either through the skin, in cyst of the liver, spleen, etc., or with the sputum in cysts of the lung.

The scolices or hydatids appear as small, white, bladder-like cysts, semitransparent and variable in size from that of a small pea (or smaller and almost microscopic in size) to that of a grape. A small thickening is easily visible to the naked eye at one of the poles, and this corresponds to the scolex or head of the larva invaginated in the cavity of the cyst. By careful manipulation the head can be evaginated, or it may be simply dissected, and under the low power of the microscope the presence of the suckers, rostellum, and hooks can be made out.

If the material to be examined consists of macerated tissue in which

scolices cannot be readily seen, or if it is merely a fluid, this should be allowed to settle either by allowing it to stand over night in a conic vessel or by centrifugalizing it for a few minutes and then examining the sediment for the presence of scolices or hooks.

If the material should contain only a few scolices or hooks, so that their presence could not be demonstrated in the small amount of sediment examined, it is recommended to add to the sediment antiformin or a solution of 10 per cent. sodium hydroxid solution, in the proportion of one part of sediment to nine parts of the digestive liquid, and boil the mixture for a few minutes. By this procedure shreds of tissue and other detritus are dissolved in the liquid, while the hooks remain unaffected. The liquid is centrifugalized for some time (five to ten minutes), and the sediment examined for the presence of hooks.

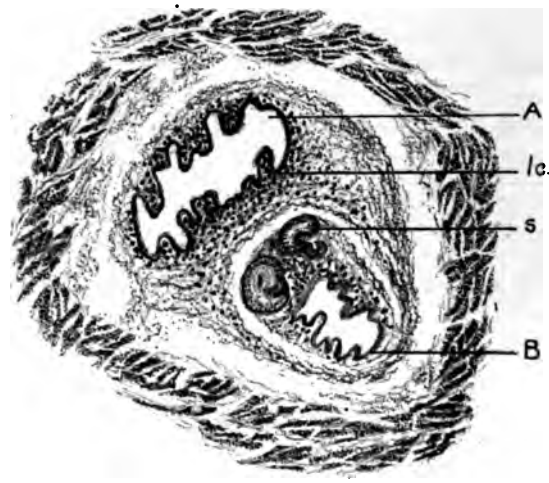


FIG. 164.—Cysticercus bovis in the heart muscle of a cow showing two sections of the larva, *A* and *B*. *Lc*, lime cells; *S*, suckers.

Examination of the tissue is made by the sectional method. A small portion of the organ, including the cyst-wall of the hydatid cyst, is fixed in formaldehyd or alcohol, mounted in paraffin, sectioned, and stained. The cyst wall and the larvæ or scolices attached to it are easily recognized.

Search for the Eggs.—In making a classification of the cestodes we have shown that these parasites are divided into two families, namely: *Dibothriocephalidæ* and *Teniidæ*, and that one of the most distinctive characteristics of the two families is the presence of the birth pore (uterine orifice or metraterm) for the discharge of the eggs in the former and the absence of it in the latter. This latter fact, therefore, explains the ease with which the eggs of *Dibothriocephalus latus*, for instance, are found in the feces, in contrast to the eggs of

T. solium, *T. saginata*, etc., which, as a rule, are rare and not uncommonly absent. It is not to be supposed, however, that the eggs of *Teniæ* may not be found in the feces, for, as a rule, disintegration of the segments occurs and the eggs are set free in the lumen of the intes-



FIG. 165.—Cysticercus fasciolaris in liver of rat. *cw*, cyst wall; *sk*, suckers; *H*, hooks.

tine, but as this disintegration is more apt to take place in the old segments, an early infestation may escape detection.

In suspected cases, therefore, it is well to examine the feces of the patient several times, at intervals of one or two weeks, for the presence of eggs and proglottides. The eggs of all *Teniæ* are small, almost

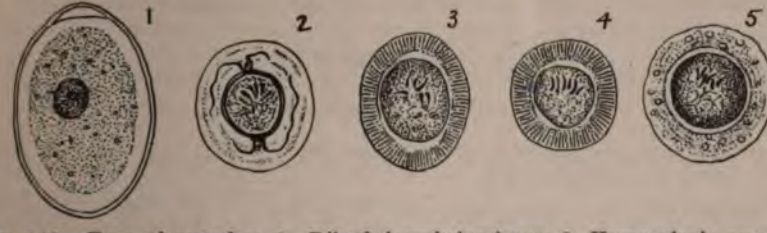


FIG. 166.—Eggs of cestodes: 1, Dibothriocephalus latus; 2, Hymenolepis nana; 3, Tenia solium; 4, Tenia saginata; 5, Dipylidium caninum.

round or slightly oval in shape, and consist of two parts—a central portion or onchosphere, which contains six hooks, and a peripheral portion or embryophore.

For all practical purposes the eggs of *Dibothriocephalus* resemble the eggs of trematodes. Like these, they are oval in shape, relatively

large in size, thin shelled, and provided with an operculum at one of the poles. As the eggs are usually discharged with the feces in the cleavage stage, they contain a mass of cleavage cells, yolk cells, and a large cell, the "germ cell," situated near the center. After remaining for some time in an external environment, and under proper temperature and moisture conditions, a ciliated larva, which resembles a miracidium, is formed within the shell, but, unlike the miracidium, it is provided with six hooks, which is characteristic of the first larval stage of all cestodes (Plate VIII and Figs. 145 and 166). In the following table the most important characteristics common to the eggs of the parasitic cestodes of man are given:

CLASSIFICATION OF EGGS OF CESTODES

Family	Characteristics		Size in Microns	Species
Taeniidæ	Provided with one membrane.	Spheric and dark.	31–38 in diameter.	*T. solium.*
		Oval and dark.	30–40 by 20–30.	*T. saginata.*
		Spheric and brown.	30–36 in diameter.	*Echinococcus granulosus.*
		Spheric and transparent.	43–50 in diameter.	*Dipylidium caninum.*
Eggs not operculated.	Provided with two membranes.	Oval and brownish.	35–45 in length. Onchosphere 8–15.	*Davainea madagascariensis.*
	Provided with three membranes.	Elliptic, round, or oval.	30–48 in diameter	*Hymenolepis nana.*
			60–85 in diameter.	*H. diminuta.*
Dibothriocephalidæ	Elliptic and brown.		70 by 45	*D. latus.*
	Elliptic and brown.		60 by 40	*D. parvus.*
Eggs operculated.	Elliptic and brown.		75–80 by 50	*D. cordatus.*
	Elliptic and brown.		63 by 50	*Diplogonoporus grandis.*

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CHAPTER XVI

NEMATHELMINTHES

ACANTHOCEPHALA. GORDIACEA

Classification.—Acanthocephala: Morphology and Structure; Life History; Classification.—Gigantorhynchus gigas.—G. moniliformis.—Gordiacea: Morphology and Structure; Life History; Classification.—Gordius aquaticus.—G. chiliensis.—Paragordius varius.—P. tricuspidatus.—P. cintus.—Parachordodes tolosanus.—P. postulosus.—P. violaceus.—Chordodes alpestris.

The Nemathelminthes are metazoa, that are usually parasitic during some part of their life cycle. The larval stage may develop in a different host or organ from that inhabited by the adult. Either the larval stage may be free and the adult worm parasitic, or vice versa. The sexes are divided. The alimentary canal is usually present and complete, although in a few species it may be atrophied in the adult (Gordiacea) or entirely absent (Acanthocephala). The respiratory organs are absent. The Nemathelminthes are tubular or filiform in shape, unsegmented, and although the surface of the body is ringed, these rings are confined to the cuticle. The true celomic cavity is usually absent. The surface of the body is free from appendages or limbs, but it may be provided with bristles or papillæ. Hooks may be present, but suckers are generally absent. One of the chief characteristics of this phylum is the almost complete absence of cilia.

Classification.—The Nemathelminthes include such parasites as the hook-worm, filaria, trichina, etc., which are the cause of serious diseases in man. The phylum is divided into three orders: Acanthocephala, Gordiacea, and Nematoda.

Order I. Acanthocephala.—The Acanthocephala are parasitic cestodiform Nemathelminthes of the intestines of the lower vertebrates, but rarely occurring in man. The anterior part of the body is provided with a retractile proboscis, somewhat resembling the rostellum in cestodes, and provided with hooks for attachment to the host. The intestinal canal is absent.

Order II. Gordiacea.—The Gordiacea are saprozoitic or free-living Nemathelminthes and but seldom parasitic. The intestinal canal is complete only in early life, but is always atrophied in the adult.

Order III. Nematoda.—The nematodes are commonly parasitic Nemathelminthes having a complicated life history. The presence of a complete alimentary canal and an absence of cilia are characteristic.

CLASSIFICATION OF NEMATHELMINTHES

Class	Characteristics	Order
Class I: Cestodiform; intestinal canal absent.	Parasitic; presence of proboscis and hooks; absence of intestinal canal.	Order I: Acanthocephala.
Class II: Intestinal canal present, either complete or rudimentary.	Usually non-parasitic. Intestinal canal complete in early life, anterior part atrophied in the adult.	Order II: Gordiacea.
	Usually parasitic. Intestinal canal always present and complete.	Order III: Nematoda.

Order I. Acanthocephala.—*Morphology and Structure.*—The Acanthocephala (Figs. 167 and 168) are elongated, cylindric Nemathelminthes found as parasites in the intestines of vertebrates, but seldom seen in man. About 200 to 300 species are known. The body is divided into proboscis, neck, and trunk.

The proboscis is a retractile, hollow structure at the anterior part of the body, provided with several rows of hooks for attachment to the host. It can be retracted into the proboscis sheath.

The neck is not always distinct; it is the point of union between the proboscis and the trunk.

The trunk or body is elongated, rounded posteriorly, and covered with a delicate cuticle which incloses the internal organs.

The Muscles.—The muscular system consists of a longitudinal and a circular layer below the cuticle, a retractile band for the lemniscus, and another for the proboscis.

Excretory System.—The excretory organs consist of a nephridial system, which begins in a three-lobed flame cell with a single nucleus (cestodes have one nucleus for each cell), and is continued by a system of capillaries that anastomose to form a closed vascular system divided into an anterior and a posterior portion.

The anterior canal system is concerned with the contraction and retraction of the proboscis, the lemniscus acting as a reservoir for the liquid.

The posterior canal system acts as a digestive apparatus, and is concerned with the digestion and circulation of digested food. Since the parasites have no intestine, food is taken by osmosis.

Reproductive Organs.—The sexes are divided. In the male the reproductive organs consist of testes, seminal vesicles, vas deferens, cement gland, or prostate and cirrus. The female organs consist of two or several floating ovaries (not attached) in the body cavity, each producing a single egg; a uterus, called the "bell," provided with

a cup-like expansion for the reception of the egg, and one small opening for the passage of the embryo into the vagina to the outside. The reproductive organs are attached to the proboscis sheath by a central ligament and by the retinaculum to the side of the body.

Life History.—The Acanthocephala, require two hosts. Fertilization, cleavage, and the larval stage take place in the body of the

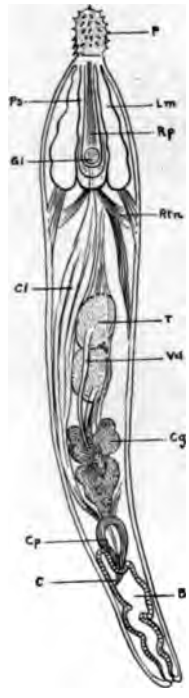


FIG. 167.

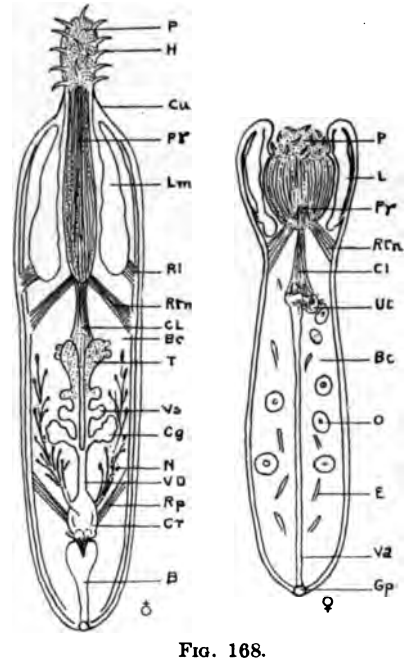


FIG. 168.

FIG. 167.—Diagram of male Acanthocephala Echinorhynchus angustatus. *P*, proboscis; *Rp*, retractor proboscis; *Ps*, proboscis sheath; *Lm*, lemniscus; *Gl*, ganglion; *Rtn*, retinaculum; *Cl*, central ligament; *T*, testes; *Vd*, vas deferens; *Cg*, cement glands; *Cp*, cirrus pouch; *C*, cirrus; *B*, bursa. (*Slightly modified after Hatschek in Hertwig, Manual of Zoology.*)

FIG. 168.—Diagram of the anatomy of an Acanthocephala Echinorhynchus ♂, male and ♀, female, the latter with proboscis retracted. *p*, proboscis; *H*, hooks; *Cu*, cuticle; *Pr*, retractor proboscis; *Lm*, lemniscus; *Rl*, retractor lemniscus; *Rtn*, retinaculum; *Cl*, central ligament; *Bc*, body cavity; *T*, testes; *Vs*, vesicula seminalis; *Cg*, cement glands; *Vd*, vas deferens; *Rp*, retractor penis; *Cr*, cirrus; *B*, bursa; *Ut*, uterus or bell; *O*, ovaries and eggs; *E*, embryo; *Va*, vagina; *Gp*, genital pore; *N*, nephridium.

female worm. The larva, which is provided with eight hooks, passes through the small opening in the uterus or "bell," thence into the the vagina, and is finally discharged through the genital opening. It now leaves the host and is carried into water, when swallowed by a water insect, such as a crustacean, it bores its way through the intestinal wall into the body of the host. Here it develops all but the

reproductive organs, and when ingested by a susceptible vertebrate, attaches itself to the intestine and becomes an adult.

Classification.—The Acanthocephala are divided into four families: (1) Echinorhynchidæ; (2) Gigantorhynchidæ; (3) Neorhynchidæ; and (4) Arhynchidæ. Human parasites have been found in only the first two families.

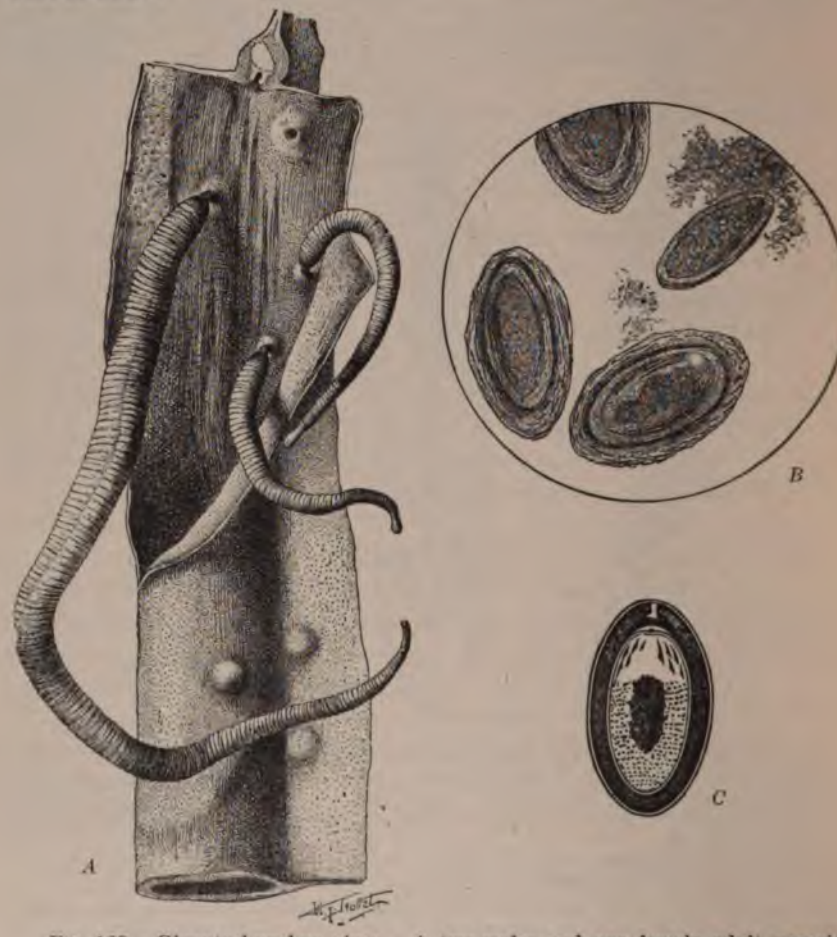


FIG. 169.—Gigantorhynchus gigas. *A*, two males and one female adult parasite attached to the mucosa of the intestine (natural size); *B*, eggs as seen in preparation, made directly from the uterus (× 250); *C*, eggs seen in the feces (× 300). (*A and B after Brumpt; C, after Perrier in Brumpt.*)

Gigantorhynchus Gigas (Goeze, 1782).—This is a parasite of the intestine of hogs, and is said to occur in man in the south of Russia (Lindeman). The male measures 5 to 10 cm. in length by 3 to 5 mm. in width. The female measures 20 to 30 cm. by 4 to 10 mm. in width. The eggs are provided with three envelops, which are common to all acanthocephala eggs, are elliptic, and measure 80 to 100μ in length.

The intermediate host is the larva, Melolantha, *Cetonia aurata* or *Lachnosterna arcuata* (Fig. 169).

Gigantorhynchus moniliformis (Bremser, 1811).—This parasite is commonly found in rats in the south of Italy. It has been found in the intestine of man (Grassi and Calandruccio). The male measures 4 to 5 cm. and the female 7 to 10 cm. The eggs are oval and measure 85 by 45μ. The body of the adult is pointed at both ends and presents a series of knobs that give the parasite a beaded appearance. The intermediate host in Europe is the *Blaps mucronata*, and in America, *Periplaneta americana*.

Echinorhynchus hominis (Lambl, 1859).—This parasite was found in the intestine of a boy.

Order II. Gordiacea.—*Morphology and Structure.*—These worms, popularly known as "horse-hair" or "hair-eels," are, like filaria, very long and slender. They bear a striking resemblance to the nematodes, but differ as to structure. They are found in ditch water, swimming freely or twining around aquatic plants. An intestinal canal is present only in early life, but is always atrophied anteriorly in the adult.

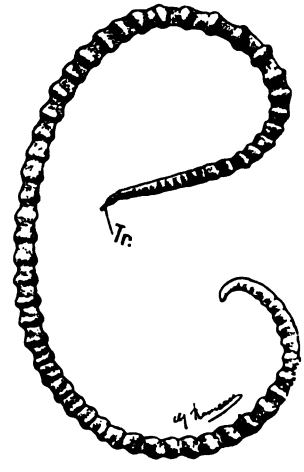


FIG. 170.—Gigantorhynchus moniliformis, slightly enlarged. *Tr*, cephalic end. (*After Brumpt.*)

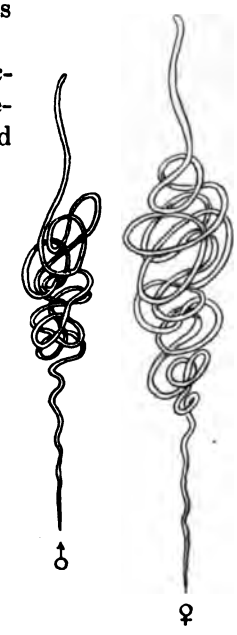


FIG. 171.—Gordius varius; ♂, male and ♀, female.

The body is covered with a well-developed, two-layered cuticle. The head is without papillæ, somewhat round, knob like, and similar in both sexes. In the female the tail may be blunt, but is usually trilobed, with the cloaca at the base; in males it is usually bilobed.

Alimentary System.—This consists of a mouth, which is plugged or atrophied in the adult, esophagus, intestine, and anus or cloaca.

Excretory System.—This is absent; there is no trace of nephridia.

Reproductive Organs.—The male reproductive organs consist of two testes, a vas deferens, and a cirrus. It has no spicule. The female organs consist of an ovary, uterus, oviduct, receptaculum seminis, atrium, and cloaca.

Life History.—The life history is complex, and requires two hosts. After copulation of the sexes the fertilization of the egg takes place in the atrium, in the body of the female, and the fertilized eggs are subsequently discharged in water as long strings. Cleavage takes place in the water and gives rise to a blastula, gastrula, and finally to a larva, which at first is inclosed in an envelop or shell, but later becomes free. The larva of Gordiaceæ is differentiated from other larvæ by being divided, by a diaphragm, into an interior part or proboscis, provided with hooks, and a body proper, or posterior part.

The larva, in the water, enters the body of an aquatic insect, not by being swallowed, for digestion would destroy it, but by boring its way through the soft part between the joints of the tibia of the insect when it rests in the water or mud. In the body of the insect the larva now drops the proboscis and becomes encysted between the muscle, where it remains dormant until the death of the fly. Entering a second host—a cricket or beetle, for instance, when it eats the decomposed fly, the larva now grows into an adult it is discharged and the cycle is repeated.

Pathogenesis.—This nemathelminth, if swallowed, has been said to cause serious and fatal diseases in man and animals, but the observations of Stiles failed to show the dangerous nature of the parasite. In man these worms are very rare and unimportant parasites.

Classification.—The Gordiacea include the family Gordiidæ, which is divided into four genera: (1) Gordius; (2) Paragordius; (3) Parachordodes; (4) Chordodes. The following are the species that have occasionally been found in man.

1. *Gordius aquaticus* (L. 1858).—Four cases of this parasite occurring in man have been reported in Europe, accompanied by abdominal and nervous symptoms, pain, vomiting, hysteric attacks, and neuralgia.

2. *G. chiliensis* (E. Blanchard, 1849).—There are not reliable sources of information regarding the true nature and occurrence of this parasite in man, such information being based on the legends of Chilian Indians in South America.

3. *Paragordius varius* (Leidy, 1851).—Four cases have been reported in man in North America. The symptoms are unimportant. The parasites were expelled per anum or by vomiting.

4. *P. tricuspidatus* (Dufour, 1828).—One case was reported in France. The parasite was extracted from the throat.

5. *P. cintus* (von Linstow, 1906).—One case was reported in man in South Africa.

6. *Parachordodes tolosanus* (Dujardin, 1842).—Four cases of this parasite in man have been reported in France and Italy.

7. *P. postulosus* (Baird, 1855).—One case was reported in Italy causing pruritus and discharge from the rectum.

8. *P. violaceus* (Baird, 1853).—One case was found in man in Italy. The parasite was lodged in the throat before expulsion.

9. *Chordodes alpestris* (Villot, 1903).—One case was found in France.

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CHAPTER XVII

NEMATHELMINTHES (Continued)

ORDER III. NEMATODA

GENERAL CONSIDERATION OF NEMATODES

History.—Morphology and Structure.—Mode of Fixation.—Habitat.—Development and Embryology.—Life History.—Mechanism of Transmission.—Pathogenesis.—Laboratory Diagnosis of Nematodes.—Treatment.—Prophylaxis.—Classification.

The nematodes are nemathelminthes having a filiform body, usually cylindric in shape, and provided, in the adult, with a complete alimentary canal. The sexes are divided. The male is provided with a single testis, and is easily differentiated from the female by its smaller size, by the strongly curved posterior extremity, and by the presence of spicules. The female opening or vulva is distinct from the anus, except in the *Cloacinæ*. The body of the nematodes is inclosed in a thick, transparent, smooth or ringed cuticle, which may be provided with hooks, spines, or lateral fins. Nematodes are usually parasitic, but free living forms are commonly encountered in moist soil, stagnant water, etc.

History.—Our knowledge of the parasitic nematodes of man probably dates back to very remote times. Hook-worms, which are a cause of tropical anemia, were perhaps known to the ancient Egyptians under the name "Heltu," mentioned in the Ebers papyrus, about 1550 B.C., the disease being then called A A A disease, but all reference to the disease appears to have been lost. Dubini, in 1838, discovered this parasite in a woman in Milan, and from that time we date our knowledge concerning the existence of hook-worms in man.

Filaria medinensis, commonly called Guinea-worm, has been known since the most remote times, and it is possible that the "fiery serpent" mentioned by Moses may have been this parasite. The name dracontiasis was given by Galen to the disease caused by this parasite.

The microfilaria of *Filaria bancrofti* was discovered in Paris by Demarquay in 1863, in the chylocele fluid of a patient from Cuba. In 1866 Wucherer found it in the urine, and in 1892 Lewis made the important discovery that the normal habitat of the worm was the blood. Bancroft, in 1876, discovered the adult female, and Borne, in 1888, found the adult male.

The knowledge of *Filaria loa* takes us back to ancient times. Its occurrence in the eye has been known since the thirteenth century in Europe, but it was not until 1770 that Mongin recorded the presence of the parasite in the visual organ. In 1891 Manson found the microfilaria in the blood of man.

As to other nematodes, perhaps of less importance, mention may be made of *Trichinella spiralis*, which was discovered by Paget in 1835 and described by Owen, although it was seen by Peacock in 1828. *Strongyloides intestinalis* was described by Norm in 1876.

Morphology and Structure.—The body of a nematode (Plate X) is usually elongate and cylindric, and covered with a heavy cuticle that makes it rigid and restricts contraction and elongation of the worm. The body is divided into head, body proper, and tail. Trichinella and Trichocephalus (Trichiuris), especially the latter, are provided with a long and characteristic neck.

The Head.—The head is usually pointed, and provided with three lips, two dorsal and one ventral, between which, and at its base, is the mouth. The lips are the seat of marginal papillæ or sense organs, which may also serve for attachment to the host and for prehension of food. In some species a pair of eyes may be seen. In certain nematodes, such as the hook-worm, the buccal cavity is provided with hooks or plates.

The Body or Trunk.—The body represents the greater part of the worm. It is commonly cylindric in shape, somewhat flattened on the ventral surface, and in some species (*Oxyuris vermicularis*) has two lateral appendages or wings at each side. The dorsal and ventral surfaces are united by a lateral margin, the lateral pillars, which run along each side for the entire length of the body. The ventral surface corresponds to the line between the ventral lips and the spicules in the male, or between the ventral lips and the anus, with the genital opening between, in the female.

The tail is pointed and contains the anus, which opens ventrally in both sexes. In the male the spicules are commonly situated in front of the anus. The tail of the male Trichinella and of the family Strongyloidæ is provided with a bursa copulatrix.

The Cuticle.—The nematodes are provided with a firm, transparent, and rigid cuticle, finely ringed, and at times with scales, spines, papillæ, or wing-like lateral expansions. Below the cuticle is the subcuticle or hypoderm, which is somewhat fibrillar or granular in character, and is situated at the dorsal and ventral median line, but more especially at each side of the body; it is thickened and forms the *lateral, dorsal*, and *ventral pillars*, to which some of the internal organs are attached.

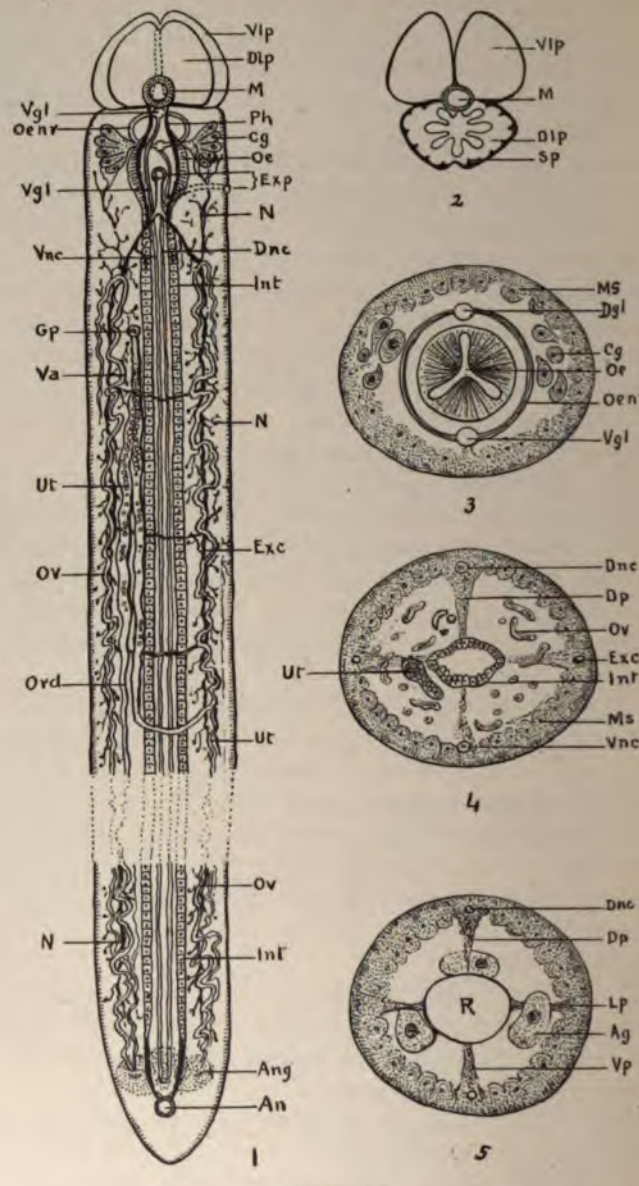


PLATE X

Diagram of the anatomy of a female nematode, Ascaris. 1, Showing the parasite as a whole; 2, the lips; 3, section through the esophagus; 4, through the middle of the body; 5, through the caudal end. *Vlp*, ventral lips; *Dlp*, dorsal lip; *M*, mouth; *Ph*, pharynx; *E*, esophagus; *Int*, intestine; *R*, rectum; *An*, anus; *Dgl*, dorsal ganglia; *Gp*, genital pore; *Va*, vagina; *Ut*, uterus; *Ovd*, oviduct; *Ov*, ovaries; *Vgl*, ventral ganglia; *Enr*, esophageal nerve ring; *Dn*, dorsal nerve cord; *Vnc*, ventral nerve cord; *N*, nephridium; *Exc*, excretory canal; *Exp*, excretory pore; *Sp*, spines; *M*, muscles; *Cg*, cervical glands; *Ang*, anal glands.

The Muscular System.—The muscle is made up of a single layer situated immediately below the hypoderm or subcuticle. It is composed of specialized muscle-cells or plates, so arranged as to constitute a valuable index in determining certain species. Three types are recognized:

1. *Polymyerial Type.*—In this type the muscle-cells or plates are fairly numerous, somewhat irregular in shape, and penetrate well down into the parenchyma and internal organs (Ascaris, Filaria, etc.).

2. *Meromyerial Type.*—The number of muscle-cells in this type is restricted to two or three between the pillars (eight to twelve plates in all). They are flat and broad, and penetrate only into the outer third of the parenchyma (Oxyuris, Ankylostomum).

3. *Holomyerial Type.*—In this type the muscle-cells are small and numerous and are close to one another, forming a narrow band immediately below the cuticle, and occupying only a small area of the outer part of the parenchyma (Trichocephalus).

Cytology.—It is characteristic of the nematodes that they have a very limited number of cells. It has been estimated that the whole nervous system of the parasites is made up of about 200 cells, and that the same number makes up the remainder of the body. The whole worm, therefore, is made up of about 400 cells in all. The animal may reach large dimensions, but this is accomplished by the growth of each individual cell. An idea as to the size of the cell may be obtained by studying the muscle-cells, which are visible to the naked eye, and may extend for several inches along the length of the animal.

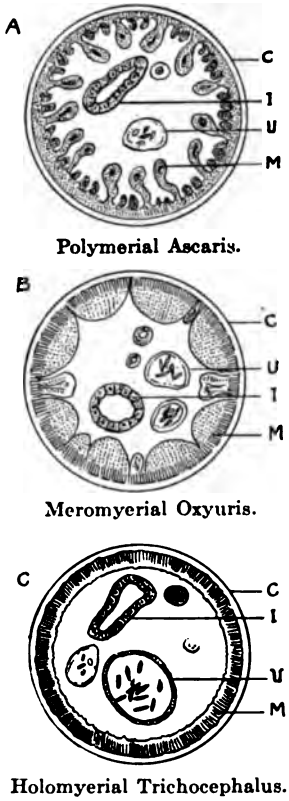


FIG. 172.—Types of muscular system in nematodes. *A*, polymyerial; *B*, meromyerial; *C*, holomyerial; *C*, cuticle; *I*, intestines; *U*, uterus; *M*, muscles.

A better illustration of the size of the cells is found in the so-called *phagocytes*. These are few in number (two to four), and are situated on the side of the body, below the cuticle. They are whitish in color, ameboid, and provided with numerous well-developed processes or pseudopods which give the cell a radial appearance. Each individual cell is of such size that it can easily be picked up with the forceps. These cells act as phagocytes and collect pigment and foreign substances.

Another peculiarity of the muscle-cells in nematodes is that they give off branches to the nerves instead of receiving them from the nerves, as is the case with other animals.

The Parenchyma.—The parenchyma, which is immediately below the muscular layer, fills the spaces between the internal organs and the interstices between the muscle plates, leaving no cavity; no true celomic cavity or peritoneum is, therefore, present in nematodes, a point that is in dispute among zoölogists. Histologically the parenchyma is made up of embryonic types of mesodermic-like cells, which are somewhat ameboid, and consist of a nucleus and a freely branched and irregular protoplasm.

Alimentary System.—The alimentary canal in nematodes is complete. It consists of a mouth, esophagus, intestine, and anus. The mouth may be terminal (Oxyuris), situated at the base of the lips (Ascaris), or located at the base of the buccal capsule (Ankylostomum). The esophagus is suctorial in function. It is thick, provided with strong muscles, and lined with chitin. The posterior part may be distended into a bulb and armed with teeth, resembling the crop of certain insects. In some cases the esophagus is constricted at the middle, forming an anterior and a posterior expansion (Rhabdites, Oxyuris), common to the larval stage of certain species.

On transverse section the esophagus is Y-shaped. It is important to remember this point since it is of great assistance in determining the position of the lips or of the hooks, plates, or pharyngeal teeth in Strongyloides produced by the fusion of one, two, or three branches of the Y. Thus, as the base of the Y corresponds to the dorsal and the branches to the lateroventral surface of the worm, it is easily remembered that Ascaris has a dorsal and two ventral lips; that Ankylostomum has a dorsal pharyngeal tooth and two lateroventral hooks (Ankylostomum) or plates (Necator) on each side.

The intestine is a straight tube that begins immediately below the esophagus; at times, however, the terminal segment of the esophagus may penetrate into the lumen of the intestine in the shape of a trilobed valve (Œsophagostomum). The intestine is brownish or black in color and ends in the anus or cloaca in the male, which opens ventrally almost at the extreme posterior end of the worm. In transverse section the intestine can easily be recognized under the microscope: it is circular or irregular in outline, somewhat centrally located, lined with columnar epithelium, and contains a brownish black or yellowish material.

The excretory system consists of a nephridial system composed of two lateral channels situated along the lateral fields, which anastomose at several points and end blindly posteriorly. Anteriorly these two lateral channels unite in a common excretory duct and end in the

nephridium or excretory pore, which opens either into the esophagus or externally. The nephridial system in nematodes contains no flame cells, but merely ameboid cells, which are few in number. The waste product is gathered by the excretory tissues (parenchyma) surrounding the nephridial system and enters the excretory tubes by osmosis. In addition, in most nematodes there exist phagocytic cells, very large in size, and about two to four in number, which are concerned with the removal of insoluble excrementitious particles and pigments from the body.

The nervous system consists of an esophageal ring and a pair of ventral ganglia from which a dorsal and a ventral cord are given off. The cords communicate along their length by a series of nerve commissures made up of alternating half-ventral and half-dorsal rings, which unite the cells of one cord with the nerve-fibers of the other. In addition, these nerve cords communicate with the muscular system by means of branches given off from the muscle-cells, and not by nerve-fibers given off to the muscle, as is usually the case with other animals.

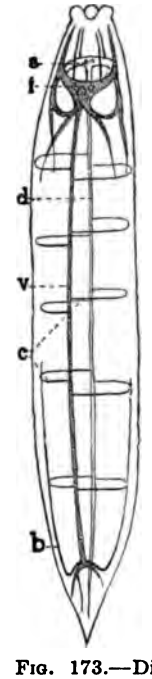


FIG. 173.—Diagram of the nervous system of a nematode. *C*, commissure; *d*, dorsal nerve; *i*, infraesophageal and *s*, supraesophageal part of nerve ring; *v*, ventral nerve. (*After Bütschli in Hertwig.*)

The Sense Organs.—Some nematodes possess a pair of eyes, but these are usually absent in the parasitic species. The sense organs common to all parasitic nematodes are the papillæ. These structures are more or less fully developed, and are seen as small elevations on the cuticle, around the lips and cephalic end of the body, along the surface of the body (*Filaria loa*), or at the caudal and around the genital opening in the male. The number and disposition of these papillæ are points in the classification.

The Reproductive Organs.—The sexes in all nematodes are divided. The male reproductive organs consist of a single tube, divisible into testes, vas deferens, vesiculæ seminales, and ejaculatory duct, which is provided with spicules and opens ventrally, at the posterior end of the body, in the anus or cloaca. The posterior part of the body may be modified into a bursa copulatrix (Strongyloidæ) or plates (Trichinella), and be provided with spines or papillæ.

The female reproductive organs consist of two closely coiled tubes, differentiated into two ovaries, from each of which an oviduct is given off; the latter are continued by the uterine tubes, which finally unite to form a short vagina. The vaginal orifice opens externally at any

of the following points: Posteriorly (Œsophagostomum); about the middle or posterior third of the body (Ankylostomum); at the junction of the anterior and middle third (Ascaris); about the middle of the body (Necator); at the anterior fifth (Trichinella); at the cephalic end (most Filaria), or into the esophagus and close to the mouth (*F. medinensis*).

Vascular System.—The vascular system is absent.

Mode of Fixation.—With a few exceptions (Ankylostoma) the organs of attachment to the host in nematodes are not so definitely specialized as in cestodes and trematodes. The papillæ around the lips, common to most nematodes, may serve as organs of attachment, but they are chiefly sense organs. Trichocephalus is provided with a long and delicate cephalic prolongation, which, by piercing the mucosa and boring deeply into the submucosa, affords an efficient means for attachment to the host. In nematodes the organs for attachment are dependent upon the habitat and degree of motility of the parasites. Thus, they are absent in nematodes that have a migratory habit, such as Ascaris, Oxyuris, Filaria, etc., and are present in those with a fixed habit, in which these organs may consist merely in an elongated cephalic end, as in Trichocephalus (Trichiuris), or be represented by specialized armatures in the form of hooks or plates, as in Ankylostomum.

Habitat.—Almost any part of the human body may serve as a medium for harboring one of the parasitic nematodes, either in the larval or in the adult stage of the worm. Thus Ascaris, Ankylostomum, Trichocephalus, etc., inhabit the intestine; Trichinella, the intestine when adult, and the muscle in the encysted larval stage; Filaria, the lymphatic, subcutaneous tissue or the blood, as the case may be. *Eustrongylus gigas* inhabits the kidneys, and *Metastrongylus elongatus* invades the lungs, etc.

Development and Embryology.—All nematodes are differentiated sexually. In most cases the fertilized egg cell is discharged by the female in the unicellular or cleavage stage—*oviparous*—as in Ascaris, Ankylostomum, etc. In other instances the embryo is discharged in the larval stage, inclosed in the egg shell—*ovoviviparous*—(Oxyuris, *Strongyloides intestinalis*); or the embyro is discharged free—viviparous—as in Trichinella and Filaria.

Taking the best known species, *Ascaris megalocephala*, as an example, the development is as follows (Plate XI):

Fertilization.—This takes place in the uterus. The egg is discharged with the feces, and undergoes further development externally.

Cleavage.—The fertilized egg divides and two cells are formed, only one of which, the *first stem cell*, carries the total number (four) of chromosomes; the other, which carries only a part of the chromo-

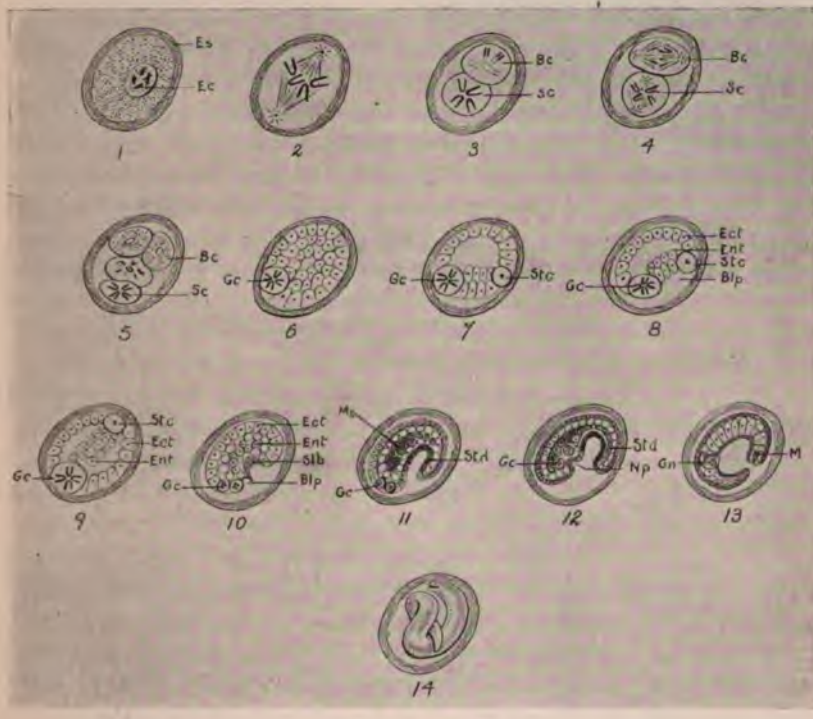


PLATE XI

Diagram of the embryology of a nematode (*Ascaris megalocephala*). 1. Fertilized egg. *Es*, egg shell; *Ec*, egg cell. 2. First division with formation of spindle. 3. First cleavage with formation of first stem cell, *Sc*, and first body cell, *Bc*. 4 and 5. Second and third cleavage stage with formation of second and third stem cells and second and third body cells respectively. 6. Blastula stage showing the germ cell, *Gc*, derived from the stem cells. 7, 8 and 9. Gastrulation and differentiation of layers (9 shown in horizontal view). *Gc*, germ cell; *Ect*, ectoblast; *Ent*, entoblast; *Stc*, stomatoblast cell derived from the ectoderm; *Blp*, blastopore. 10, 11, 12 and 13. Larval stage formation. *Blp*, blastopore disappearing; *Stb*, stomatoblast formed from stomatoblast cell; *Std*, stomodeum or primitive mouth formed by invagination of the stomatoblast; *M*, mouth from stomodeum. *Ms*, mesoblast. 14. Fully formed larva enclosed in the egg shell.

somes, is called the *first body cell.* A second division now takes place: first the first body cell and then the first stem cell divide, so that a three- and then a four-celled stage are produced, and the *second body cell* and *second stem cell,* respectively, are formed; only the latter carries the complete number of chromosomes. By subsequent division the *third* and *fourth body cells* and the *third* and *fourth stem cells* are formed. Only the last stem cell carries the complete number of chromosomes, whereas the previously formed stem cell throws them off.

At this stage the cleavage has resulted in the production of about ten or more cells. The fourth stem cell is called the *primitive germ cell,* and from this the gonads develop, whereas the embryonic layers are derived from the body cells. The embryonic layers, at this stage, are not, of course, differentiated, but the "anlage" for their develop-

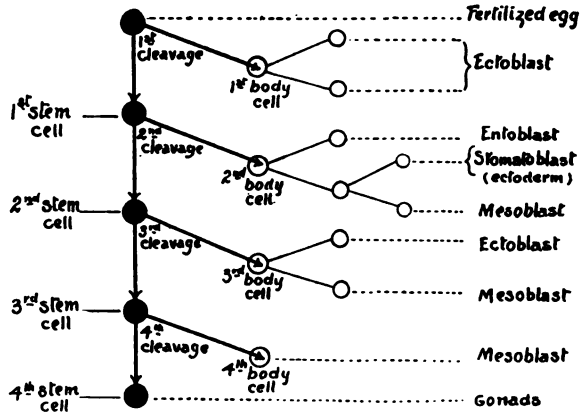


FIG. 174.—Sketch showing the origin and development of the different layers and organs of a nematode (*Ascaris megalocephala*) from the fertilised egg.

ment is already formed. Thus the *ectoblast* is derived from the first and part of the second and third body cell; the *stomatodeum* develops from one of the subdivisions of the second body cell; the *mesoblast* springs from part of the third and the whole of the fourth body cell, and the *en oblast,* from part of the second body cell, as shown in the accompanying diagram (Fig. 174).

Blastula Stage.—Cleavage is followed by the blastula stage, by invagination and gastrulation. At this stage differentiation of the layers begins.

Gastrula Stage.—The gastrula is produced by invagination or ingrowth of the blastula and the formation of the *blastopore,* with the germ cell at one pole and the *stomatoblast cell* at the other. In this stage the ectoblast and the entoblast are well differentiated. Further differentiation now takes place: the blastopore becomes obliterated, and the stomatoblast cell gives rise to the *stomatodeum* and finally

to the *mouth;* the germ cell divides and gives rise to *two germ cells*, one of which grows into the *mesoblast* and the other into the *gonads;* the ectoderm gives rise to the beginning of the *nephridium*. The embryo now elongates and passes into the larval stage.

The Larval Stage.—No true free larval stage is believed to occur in *Ascaris megalocephala*, as the embryo is inclosed in a protective shell of the egg, which, under the microscope, appears as an elongated mass differentiated into three rows of cells, all ectodermic; on close examination, however, the *stomatodeum* or mouth anteriorly, and the *rectocele* posteriorly, may be seen and the germ cells or gonads may be recognized inside.

The cuticle is derived from the ectoblast. The nuclei of the cells accumulate at two lateral lines, leaving one part (the cuticle) without nuclei, and the other (the subcuticle) with nuclei.

The digestive tract is derived from the entoblast, by the formation of a tube that finally forms the intestinal canal. The mesoblast also contributes to the formation of the digestive system.

The nephridium is likewise derived from the ectoblast, which begins in the nephridial pore, but the remainder as two lateral lines, is probably derived from the mesoblast.

The muscles are derived from the mesoblast, which strips off and forms two lateral bands or muscle-plates.

Body Cavity.—There is no true body cavity in nematodes.

Reproductive Organs.—The ovaries and testes are derived from the gonads and mesoblast.

Life History—The life history of some nematodes appears to be very simple, or is believed to be so, for we are probably not thoroughly acquainted with all the details; in others, however, the life history is most complicated.

As previously stated, nematodes are either oviparous, those that discharge the egg before a visible embryo is formed (Ankylostomum, Ascaris, Trichocephalus, etc.), or viviparous when the embryo is formed in the uterus and discharged free (Trichinella and Filaria). As a rule, all viviparous nematodes require an intermediate host for their complete development. As to the oviparous, those with a thin-shelled egg, the larva hatches outside, and after molting, enters the definite host and attains the adult stage (Ankylostomum). Those with thick-shelled eggs have no free larval stage and hatch in the host (Ascaris, Trichocephalus). According to F. H. Stewart, the life history of *Ascaris lumbricoides* requires an intermediate host, the rat (*Mus decumanus* or mouse, *M. musculus*).

All nematodes are not parasites, a large number of species living a saprozoic existence in nature. Some are facultative parasites (*Strongyloides intestinalis*) and others are obligatory parasites, either during

a certain period of their existence (Ankylostomum) or during their entire life (Filaria). Between these two types all possible adaptations are found.

The parasitic nematodes of man may be grouped into two classes: A. Those that develop without an intermediate host, and B, those that require an intermediate host.

A. Those developing without an intermediate host are, as a rule, oviparous, excepting perhaps, *Strongyloides intestinalis*, in which the embryo is formed in the uterus, but others hatch outside. Three modes of development may occur in this group:

1. Those nematodes in which the parasitic existence is apparently not essential and which may be regarded as merely occasional parasites of man, such as *Strongyloides intestinalis*. This worm displays an alternation of generation (heterogeny); it leads a saprozoic existence as a free-living form (rhabditic) in the soil, where it undergoes sexual reproduction, but in the larval stage it may occasionally enter the body of man or animals through the skin or through the mouth, and become a parasite of the intestines (*Strongyloides intestinalis*).

Only the female forms have been found as parasites in the intestine, and this phenomenon is explained either by the worm being hermaphroditic, in which a degeneration of the male organs occurs early in life, or by a very rapid maturation and death of the male after copulation.

2. Those nematodes better adapted to a parasitic existence, such as *Ankylostomum*, pass the greater part of their lives as parasites in the intestine, when grown to adult form The larva in the soil has only a short free-living existence.

3. Those parasitic nematodes of the intestine without a free larval stage (Trichocephalus and Oxyuris) are parasitic during the whole of their lives. The eggs are discharged with the feces, and, like Ankylostomum, they develop outside, though the embryo remains inclosed in the shell of the egg until it is swallowed by the host, when it hatches in the intestine.

B. The nematodes which require an intermediate host are as a rule viviparous, and in these also three possibilities may occur:

1. The worm is a parasite in the adult stage in man and is also a parasite in the larval stage in the intermediate host, usually an invertebrate, with a short free larval stage between, as is the case with *Filaria medinensis*.

2. Parasitic nematodes without a free larval stage. The embryo is transmitted directly to the intermediate host, where it undergoes preparatory development for its entrance and maintenance in the primary host, as is the case in *Filaria bancrofti*.

3. Those nematodes in which the parasitic habit is so fully developed that they not only do not have a free larval stage, but the larvæ

undergo preparatory development in the tissues of the same host, as is the case in Trichinella. In Trichinella the necessity for a secondary host has disappeared, for although the rat acts as the intermediate host for the transmission of the parasite to the hog, and the hog serves to transmit it to man, this does not mean that the same hog cannot be reinfected, if made, experimentally, to swallow its own infested flesh containing the encysted embryos of the parasite. The author has succeeded in reinfecting white rats experimentally, by compelling these animals to swallow their own infested flesh.

Mechanism of Transmission.—The transmission of a parasitic nematode to another host may be direct, without the medium of an intermediate host, or indirect, through an intermediate host. In the direct form of transmission, which is common to most oviparous varieties, two possibilities may arise: (*a*) The parasite may be transmitted either as an embryo inclosed in the egg or (*b*) it may be transmitted in the free larval stage. The former is common to those nematodes, that have a thick-shelled egg, such as Trichocephalus (Trichiuris) and Oxyuris, and the latter to those with thin-shelled eggs, as Ankylostomum and Strongyloides.

Pathogenesis.—Some parasitic nematodes, such as Trichiuris, Strongyloides, and Ascaris, when not present in very large numbers, may inhabit the intestine of man without giving rise to any appreciable morbid changes in the host. Other nematodes are known to be the cause of important diseases in man, as, for example, the hook-worm, which is the cause of ankylostomiasis or tropical anemia; Filaria, the cause of filariasis and elephantiasis, and Trichinella, the cause of trichinosis. It should be remembered, however, that the mere presence of a few of these parasites in man may not give rise to any appreciable symptoms, and that for the manifestations of the disease which they produce, besides the degree of infestation, the normal resistance and the condition of the host in general are important factors.

Laboratory Diagnosis of Nematodes.—The laboratory diagnosis of nematodes, like that of cestodes and trematodes, consists in the finding of the adult, the eggs, or the larva of the parasite, as the case may be.

Search for the Adult Parasite.—The thread-like shape common to all nematodes makes their recognition very easy. Certain species which inhabit the subcutaneous tissue, such as *Filaria medinensis* and *F. loa*, are readily detected, since they may be seen or felt under the skin. Likewise the relatively large size and red color of *Eustrongylus gigas*, which inhabits the pelvis of the kidney; the characteristic shape of *Ascaris lumbricoides;* the hook-like appearance of Ankylostomum, which inhabits the duodenum, and the whip-like shape of

Trichiuris, found in the cecum, make the recognition of these worms quite easy.

The finding in the intestine of certain nematodes that have a wandering habit, such as Oxyuris, and more especially Trichinella, without the aid of the microscope or a magnifying lens, is attended by some difficulty, since the small size of these parasites may lead them to be mistaken for vegetable fibers and other detritus of the intestinal tract.

As the greater percentage of the parasitic nematodes of man are found in the intestine, examination of the feces should be made as a routine procedure in the diagnosis of all suspected cases. The material for examination should be collected, when possible, from the second stool passed after the administration of a purgative. The feces, as commonly brought to the laboratory, are usually of normal consistence; they should first be softened and then suspended in an excess of antiseptic solution, after which they should be washed through a fine sieve or screen, the meshes of which should be 0.5 to 1 mm. square, or, better, through a double layer of gauze. The sediment should be collected and spread in a tray containing a sufficient amount of a 4 per cent. solution of formaldehyd or 1 : 1000 bichlorid, and examined with a magnifying lens against a dark or black ground. All suspected particles should be carefully removed and placed on a slide or watch crystal, and examined under the microscope for identification.

In making an autopsy it will greatly facilitate both the rapid finding and the identification of the suspected parasite to keep in mind the common habitat of the worm in question. Thus, of the parasites of the intestine, Trichinella and Ankylostomum are found in the duodenum or upper part of the small intestine; Ascaris in the jejunum; Trichiuris in the cecum; Oxyuris either in the lower part of the small intestine, when young, or in the large intestine, rectum, or anus, and in women in the external genitalia and vagina, when adult. *Eustrongyloides gigas* is found in the pelvis of the kidney and occasionally in the peritoneum; *Filaria medinensis* and *F. loa* are found under the skin, and *F. bancrofti* is seen in the lymphatics of the pelvis and the groin.

Search for the Eggs.—The laboratory diagnosis of all the parasitic nematodes of the intestine, with the exception of Trichinella, may be made by finding the eggs in the feces. If possible, the material should be collected during an attack of diarrhea or from the second stool passed after a purgative has been administered, as previously stated. Thin, fresh cover-glass preparations are made and examined under the microscope, first with the low power, for the detection of the egg and then with the high power, if desired, for identification. As a rule,

this procedure suffices in most instances, especially if two or more preparations are systematically examined by the aid of a mechanical stage.

If a negative result is obtained, a small quantity of the feces may be softened and suspended in an excess of water, thoroughly shaken, centrifugalized, and the sediment examined. Instead of water the material may be suspended in an excess of a solution of calcium carbonate, the specific gravity of which is 1.060, centrifugalized, and fresh cover-glass preparations made of the material collected from the top of the liquid (Bass). This method is based on the principle that certain eggs have a specific gravity lower than 1.060, and float on the surface of the liquid. The method has been especially recommended for the finding of eggs of Ankylostomum. In the writer's experience, however, this procedure has not been found very satisfactory, except when the material happened to contain eggs in sufficient number, when the direct and simpler procedure also gave a satisfactory result.

The eggs of Ascaris are oval, thick shelled, and when recently passed with the feces, are covered with a delicate, gelatinous membrane on the outside. This membrane, however, may be absent.

The eggs of Trichiuris are dark brown in color, thick shelled, and provided with a knob at each pole.

The eggs of Oxyuris are thick shelled, somewhat light or brownish in color, and flattened on one side *i.e.*, bean shaped.

The eggs of Ankylostomum and *Strongyloides intestinalis* are thin shelled. In addition to this characteristic, the eggs of Ankylostomum contain from four to eight cleavage cells, and those of Strongyloides contain a preformed embryo. In this the eggs are greenish in color, and not uncommonly appear in short chains, made up of from two to eight eggs inclosed in a transparent thin sheath.

The eggs of *Eustrongylus gigas* are oval in shape and provided with knobs at each end. The shell is very thick, and covered with elevations that give the egg a mosaic appearance.

Search for the Larval Stage.—The larva of some nematodes, such as Ankylostomum, may readily be found in the soil of mines and infected districts. It may also be present in the feces when these are exposed to the outside environment for some days or weeks at a warm temperature, and under proper conditions of moisture. In the early stages, either when still inclosed in the shell or shortly after hatching the larva may be recognized as a slender body provided with a bulbed esophagus (rhabditiform). After the first molt the esophagus becomes cylindric (strongyloid), and the larva is provided with an embryonic sheath closely applied to the cuticle. At this stage the larva exhibits a sluggish motility, commonly oscillating in character.

The larva of *Strongyloides intestinalis* may also be found in the

soil or in the feces under similar conditions to the Ankylostomum. Trichiuris, Oxyuris, Sclerostomum, Œsophagostomum, etc., are not known to have a free larval stage.

The embryo of viviparous parasitic nematodes, such as Filaria, and Trichinella, is never free. Microfilaria is found in the blood, and the Trichinella embryos are encysted in the muscles. Microfilaria are discovered by examining a fresh cover-glass preparation made from the peripheral blood under the low power of the microscope, preferably at night for *Filaria bancrofti*, and at noon for *F. loa*. The most satisfactory results were obtained by examining larger quantities of blood. The technic consists in collecting from five to ten drops of blood from the finger in about 5 c.c. of a 2 per cent. acetic acid solution; the mixture is shaken, centrifugalized, and the sediment examined. The microfilaria, of course, are killed by this treatment, but their characteristic shape and appearance make them recognizable without difficulty. The advantage of this method consists in the fact that the microfilaria are detected in the peripheral blood in both cases (*F. bancrofti* and *F. loa*) at all hours of the day and night. (For details see pages 409, 415, 424, 427, 428.)

At autopsy the embryos of Trichinella may be found in the mucosa of the duodenum, in the peritoneal cavity, in the blood of the heart, or encysted in the muscle. During life, the examination consists in removing a piece of muscle, preferably of the fibers near the tendons, placing the material in a little water between two slides, and examining it under the low power of the microscope. The characteristic shape of the cyst containing the embryo renders its recognition easy.

Treatment.—The treatment in parasitic nematodes in general is dependent upon the kind of parasite present as well as upon the locality inhabited by the worm. Certain nematodes, such as *Filaria bancrofti*, may be said to be beyond reach of available medication. The fact that this worm inhabits the lymphatics of the pelvis renders it immune to any of the known medicinal or surgical measures directed against it. Similarly the microfilaria in the blood appears to be refractory to any form of medication.

The peculiar habitat of *Filaria medinensis* and *Filaria loa*, in the subcutaneous tissue permits them to be easily detected and removed by surgical measures.

The parasitic nematodes of the intestine may be divided into two groups—those that can usually be dislodged or detached, as the case may be, and expelled by medication, and those that, as a rule, are known to be refractory to treatment. To the former group belong Ankylostomum, Ascaris, Oxyuris, etc., and to the latter, *Strongyloides intestinalis* and especially Trichiuris. The extremely long cephalic end of the last-named parasite bores its way deep into the submu-

cosa and gives the worm a very efficient means of attachment and protection.

Several drugs have been recommended for the treatment of intestinal parasites, but none can be regarded as a specific. The following are among the preparations usually employed.

Ethereal extract of male-fern	
Chloroform	of each 1 dram
Castor oil	1½ ounces

This is to be taken in the morning on an empty stomach, and followed two hours later by an ounce of sodium sulphate in one pint of a saturated solution of chloroform in water, divided into four doses, one being taken every fifteen minutes. The treatment is repeated every two or three days, and continued for from eight to ten days.

Another formula especially recommended for *Ascaris lumbricoides* is the following:

Santonin	½ grains
Castor oil	1½ ounces

Santonin is given in the proportion of one-tenth of a grain for each year of the child's age, and usually gives good results, but should be repeated after one or two weeks if necessary.

Still another remedy is:

Thymol	1 dram

Finely pulverized thymol is taken in capsules in six doses of ten grains each every half-hour. As the thymol is soluble in alcohol and oils, and when absorbed may give rise to severe toxic symptoms, the patient should avoid the use of alcohol and fats in any form during the treatment. The mode of procedure is as follows:

The day before the thymol is administered the patient should eat a very light supper, preferably of milk, and a mild laxative should be taken on retiring. The next morning ten grains of thymol should be given every half hour until six doses have been taken, and three to four hours after the last dose a saline purgative should be administered.

During the afternoon skimmed milk and bread may be allowed, with a very light supper in the evening, consisting of milk, bread, coffee, and one or two soft-boiled eggs.

This treatment is especially recommended for Ankylostomum and is sometimes very effective, but should be repeated every two weeks or every month, if required, where the condition of the patient permits it. *No case should be regarded as cured until, upon repeated examination, no eggs are found in the feces.*

From the foregoing it may be seen that none of these remedies can be regarded as specific, since their beneficial effects are dependent

merely upon the prolonged action of the drug, as the result of which the chemistry of the intestinal tract is sufficiently altered to render it an unfavorable environment for the parasite.

Prophylaxis.—The prophylactic measures to be directed against infestation of certain nematodes, such as Filaria, which are transmitted by insects, consist in avoiding the bites of mosquitos in localities where the disease is known to be prevalent.

For Trichinella, which is transmitted in the encysted embryonic form, as found in the muscles of the hog, care should be taken to avoid the use of improperly cooked meats. It is important to remember that infestation by this parasite usually takes place through the use of ham or sausage.

Infestation of the intestines by the parasitic nematodes that have a direct form of transmission, such as Ascaris, Trichiuris, Oxyuris, and Ankylostomum, etc., may be prevented by observing the following precautions: Proper disinfection of the feces; purification of the water supply; sanitation of the soil in main districts; and especially disinfection of the hands before meals. In the case of Ankylostomum and *Strongyloides intestinalis*, etc., in which the larva penetrates the skin, the prophylactic measures recommended are the wearing of proper shoes and the protection of the exposed parts of the body, such as the hands, arms, legs, knees, etc., in infected localities.

Classification.—The nematodes may be divided into two groups: The free-living and the parasitic species. To the first group belongs the family *Enoplidæ*, which is of no interest in human parasitology. The parasitic group comprises the following families: (1) *Anguillulidæ;* (2) *Angi stomidæ;* (3) *Gnathostomidæ;* (4) *Strongylidæ;* (5) *Ascaridæ;* (6) *Trichinellidæ;* (7) *Filaridæ*, and (8) *Mermithidæ*.

Of these, the *Anguilludiæ*, *Gnathostomidæ*, and *Mermithidæ* may be said to be unimportant, since they contain only a few and occasional parasitic species of man. The same may be said of the *Angiostomidæ*, which live as sporozoa in the soil and are only occasionally found as a parasite of man. Such is not the case, however, with the *Ascaridæ*, *Strongylidæ*, *Trichinellidæ*, and *Filaridæ*, which are obligatory parasites, and contain such species as *Ascaris lumbricoides*, *Ankylostomum duodenalis*, *Trichiuris* (*Trichocephalus*) *trichiurus*, *Trichinella spiralis*, and a number of *Filariæ* that are the cause of important diseases in man.

The foregoing classification is based upon morphologic and biologic characteristics peculiar to each family, which may be summarized as follows:

Family I. Anguillulidæ.—Nematodes, very small, usually free living, mouth armed with a tooth or spine, the esophagus having a double dilatation.

Genus 1. *Anguillula* (Ehrenberg, 1826).—Mouth very small, esophagus has two dilatations. Male with bursa; female with the vulva at posterior part of the body; uterus asymmetric.

Species: *Anguillula aceti* (Müller, 1783).

Genus 2. *Anguillulina* (Gervais and Beneden, 1859).—Anguillulinæ are provided with a spine in the oral cavity. Male bursa without papillæ. Uterus asymmetric.

Species: *Anguillulina putrefaciens* (Kuhn, 1879).

Genus 3. *Rhabditis* (Dujardin, 1845).—Small anguillulidæ; oral cavity without papillæ; absence of lateral ridges.

Species: *Rhabditis niellyi* (Blanchard, 1885).

Genus 4. *Leptodera* (Dujardin).—Mouth with two, three, or six lips. Male with or without bursa; two equal spicules and three preanal papillæ. Female with long pointed tail.

Species: *Leptodera pellio* (Schneider, 1866).

Family II. Angiostomidæ.—Nematodes with heterogony; a free living bisexual and a parasitic (probably hermaphrodite) form.

Genus: Strongyloides (Grassi, 1879).—Parasitic form (*S. intestinalis*) has an unarmed mouth; esophagus long and cylindric. The non-parasitic form has a short esophagus with a double dilatation. Male with spicules of equal size.

Species: *Strongyloides intestinalis* (Bavay, 1876).

Family III. Gnathostomidæ.—Nematodes with fine spines over the body; mouth provided with two lips; parasitic in the stomach of dogs, cats, pigs, and oxen.

Genus: Gnathostoma (Owen, 1836), with the charters of the family (*G. siamense*).

Family IV. Strongylidæ.—Nematodes having a cylindroid, rarely a filiform body. Male provided with a bursa copulatrix and two equal spicules. Female with single or double ovary; oviparous or ovoviviparous. The family contains the genera *Eustrongylus* (Diesing, 1851) (Dioctophyme), *Strongylus*, *Metastrongylus*, *Trichostrongylus*, *Ankylostoma*, *Necator*, *Triodontophorus*, *Œsophagostoma*, and *Physaloptera*, which are grouped by Railliet into three subfamilies.

Subfamily 1. *Eustrongylidæ* (Railliet).—Mouth unarmed, bursa copulatrix, without ribs or bands.

Genus: Eustrongylus.—Very large strongylidæ; body cylindric; mouth with six papillæ. Male with a collar or cup-shaped bursa provided with one spine. Female with a single ovary; vulva in anterior part of the body.

Species: *Eustrongylus gigas* (Diesing, 1851) (*Strongylus gigas*, Rudolphi, 1802).

Subfamily 2. *Stronglinæ* (Railliet).—Strongylidæ with mouth unarmed and bursa copulatrix provided with ribs or bands.

Genus 1. *Strongylus* (Müller).—Mouth with or without papillæ; esophagus dilated. Male with bursa copulatrix provided with two equal spicules. Female with vulva situated in the posterior part of the body.

Species: *Strongylus gibsoni* (Stephens, 1909).

Genus 2. *Metastrongylus.*—Mouth with six papillæ; slightly developed esophageal bulb. Female ovoviviparous, two ovaries, and a tapering posterior end.

Species: *Metastrongylus apri* (Gmelin).

Genus 3. *Trichostrongylus* (Looss, 1905).—Body tapered anteriorly; three lips; esophagus long; male with spoon-like spicules; female with vulva in the posterior half of the body.

Species: *Trichostrongylus instabilis. T. probolurus; T. vitrinus.*

Subfamily 3. *Sclerostominæ* (Railliet).—The distinctive characteristic of this subfamily is the presence of hooks or plates in the mouth and a bursa copulatrix provided with ribs. To this subfamily belongs the hook-worm, which is the cause of ankylostomiasis in man. It comprises the following genera:

Genus 1. *Ankylostoma* (Dubini, 1843).—Head abruptly truncated, bent posteriorly, and armed with two pairs of strong hooks. Male bursa three lobed. Female with vulva behind the middle of the body.

Species: *Ankylostomum duodenalis* (Dubini, 1843).

Genus 2. *Necator* (Stiles, 1903).—Head armed with two pairs of semilunar plates. The bursa in the male is bilobed. The vulva in the female lies in the anterior part of the body.

Species: *Necator americanus* (Stiles, 1902).

Genus 3. *Triodontophorus* (Looss, 1901).—Head with a thick-walled oral cavity provided with three teeth. Male bursa serrated at the edges. In the female the vulva is situated at the posterior end and in front of the tip of the tail.

Species: *Triodontophorus diminutus* (Railliet and Henry, 1905).

Genus 4. *Œsophagostoma* (Molin, 1860).—Mouth with a chitinous ring provided with six papillæ. Male bursa with two equal spicules. Female with two ovaries; vulva near the anus.

Species: *Œsophagostoma brumpti* (Railliet and Henry, 1905).

Genus 5. *Physaloptera* (Rudolphi, 1819).—Mouth usually with two lips, each with papillæ and teeth. Male with posterior lanceolate end due to cuticular expansions; bladder-shaped bursa; spicules unequal. Female with two ovaries; vulva anterior.

Species: *Physaloptera mordens; P. caucasica.*

Family V. Ascaridæ.—Nematodes with three oral papillæ or lips, one dorsal and two ventral. Male with one or two spicules. Female with two ovaries.

Genus 1. *Ascaris.*—Three large lips, one dorsal and two ventral. Male with two equal spicules and several anal and postanal papillæ. Vulva about the junction of the anterior and middle third of the body.

Species: *Ascaris lumbricoides* (Linnæus, 1758); *A. texana* (Smith and Goeth, 1904); *A. maritima* (Leuckart, 1876).

Genus 2. *Toxascaris.*—Anterior end bent dorsally; esophagus simple; lips club shaped. Male with a tapering cuticular tail; six pairs of postanal papillæ. Testis in anterior part of posterior third of body. Female with vulva about the middle of the body. Eggs oval and smooth.

Species: *Toxascaris canis* (Werner, 1782).

Genus 3. *Belascaris.*—Anterior end of body bent ventrally; esophagus bulbed. Male with tail provided with four pairs of papillæ, two ventral and two lateral; testes in the anterior half of the body. Female with vulva situated in the anterior part of the body.

Species: *Belascaris mystax.*

Genus 4. *Oxyuris.*—Three very small lips; esophagus with a distinct dilatation. Male with a curved posterior end, a single spicule, and two pairs of preanal papillæ. Female with tapering cuticular tail; vulva in anterior end of body.

Species: *Oxyuris vermicularis* (Linnæus, 1767).

Family VI. Trichinellidæ.—Nematodes with long and slender cephalic end, club or whip-like in shape; mouth without papillæ; esophagus very long.

Genus 1. *Trichiuris* (Buttner, 1761).—Large Trichinellidæ. Anterior part of the body very long and thread-like; anus terminal. Male with spirally rolled posterior end; a single spicule. Female oviparous; one ovary; vulva at the junction of the thinner and thicker part of the body.

Species: *Trichiuris trichiurus* (Linnæus, 1771).

Genus 2. *Trichinella.*—Very small nematode; thin and hair-like body. Male with two caudal, flap-like appendages, with the cloaca between. Female viviparous; vulva in anterior part of body.

Species: *Trichinella spiralis* (Owen, 1835).

Family VII. Filaridæ (Braun, 1895).—Long, filiform nematodes of uniform diameter. Mouth terminal and provided with two lips; esophagus long and slender; anus subterminal. Male with recurved tail provided with papillæ or lateral alæ. Female larger than the male; viviparous; vulva situated anteriorly. Uterus usually double.

Genus: Filaria (Müller, 1787).—With the characteristics of the family.

Species: *Filaria bancrofti* (Cobbold, 1877); *F. loa* (Guyot, 1778); *F. perstans* (Manson, 1891); *F. medinensis* (Velsch, 1674), etc.

CLASSIFICATION OF THE PARASITIC NEMATODES OF MAN

Order	Family	Differential Characteristics	Genus	Species	Average Size	Habitat
NEMATODA. Nemathelminthes. Body filiform and cylindric. Complete alimentary canal. Sexes separate. Commonly parasitic.	I. *Anguillulidæ:* Small, commonly free living; esophagus with two dilatations.	Male with bursa. Female with vulva posteriorly.	Anguillula.	*A. aceti.*		Bladder (?)
		Mouth with spines. Uterus asymmetric.	Anguillulina.	*A. putrefaciens.*		Stomach (?)
		Mouth with papillæ.	Rhabditis.	*R. niellyi.*	♂1.0 mm. ♀3.0 mm.	Skin.
		Mouth with lips. Male with three preanal papillæ.	Leptodera.	*L. pellio.*	♂1.0 mm. ♀1.1 mm.	Skin.
	II. *Angiostomidæ:* Nematodes with heterogeny.	Mouth armed. Parasitic and free living.	Strongyloides	*S. intestinalis.*	2.2 mm.×34μ.	Small intestine.
	III. *Gnathostomidæ:* Mouth with two lips.	Spines over the body.	Gnathostoma.	*G. siamense.*	♀ 9×1 mm.	Stomach and intestine.
	IV. *Strongylidæ:* Male with bursa copulatrix Female oviparous or ovoviviparous	Mouth unarmed. Male with collar-shaped bursa. Female with bursa anteriorly.	Eustrongylus.	*E. gigas.*	♂ 30 cm.×5 mm. ♀ 60 cm.×8 mm.	Kidney.
		Mouth unarmed. Male bursa with ribs. Female with vulva posteriorly.	Strongylus.	*S. gibsoni.*	♂ 21×0.4 mm. ♀ 25×0.6 mm.	Intestine.
		Mouth with six lips. Esophagus slightly bulbed.	Metastrongylus.	*M. apri.*	♂18 mm. ♀30 mm.	Lungs.
		Mouth with three lips. Esophagus long. Male with spoon-like spicules. Female with vulva posteriorly.	Trichostrongylus.	*T. instabilis.*	♂ 4.5×0.08 mm. ♀ 5×0.09 mm.	Intestine.
				T. probolurus.	♂ 4.5×0.08 mm. ♀ 5×0.1 mm.	Intestine.
				T. vitrinus.	♂ 5×0.08 mm. ♀ 5.5×0.1 mm.	Intestine.
		Mouth armed with two pairs of hooks. Male bursa trilobed.	Ankylostoma.	*A. duodenalis.*	♂ 10×0.5 mm. ♀ 12×0.8 mm.	Intestine.
		Mouth armed with two pairs of chitinous plates. Male bursa bilobed.	Necator.	*N. americanus.*	♂ 8×0.3 mm. ♀ 9.5×0.6 mm.	Intestine.
		Mouth armed with three teeth. Male with bursa at tail.	Triodontophorus.	*T. diminutus.*	♂ 9×0.5 mm. ♀ 11×0.6 mm.	Intestine.

V. *Ascaridæ:* Mouth with three lips. Esophagus bulbed. Male with one or two spicules. Female with two ovaries.	Male with two spicules. Female with vulva at junction of anterior and middle parts of body.	Ascaris.	*A. lumbricoides.*	♂ 18 cm. × 3 mm. ♀ 30 cm. × 5 mm.	Intestine.
			A. lexana.	♀ 59 × 1.2 mm.	Intestine.
			A. maritima.		Intestine.
	Anterior end bent dorsally. Male with tapered posterior end. Female with vulva at middle of body.	Toxascaris.	*T. canis.*	♂ 5.5 cm. ♀ cm.	Intestine.
	Anterior end bent ventrally. Male with four pairs caudal papillæ. Female with vulva anteriorly.	Belascaris.	*B. mystax.*	♂ 5 mm. ♀ 7 mm.	Intestine.
	Body with lateral circular ridges. Male with single spicule. Female with tapered tail; vulva posteriorly.	Oxyuris.	*O. vermicularis.*	♂ 4 × 0.4 mm. ♀ 10 × 0.6 mm.	Intestine.
VI. *Trichinellidæ:* Whip-like in shape; esophagus very long.	Male with single spicule. Female oviparous. Vulva at junction of thin and thicker parts of body.	Trichiuris.	*T. trichiurus.*	♂ 40 mm. ♀ 48 mm.	Intestine.
	Body very small. Male with two cones or flaps at the tail. Female viviparous; vulva anteriorly.	Trichinella.	*T. spiralis.*	♂ 1.5 × 0.04 mm. ♀ 3.5 × 0.06 mm.	Intestine.
VII. *Filaridæ:* Body long and filiform. Viviparous.	Sexually mature. Mouth with two lips. Male with tail spirally curbed. Female with vulva anteriorly.	Filaria.	*F. bancrofti.*	♂ 40 × 0.1 mm. ♀ 90 × 0.25 mm.	Lymphatics and blood.
			F. loa.	♂ 30 × 0.3 mm. ♀ 60 × 0.4 mm.	Subcutaneous tissue and blood.
			F. perstans.	♂ 45 × 0.06 mm. ♀ 9.75 × 0.12 mm.	Mesentery and blood.
			F. medinensis, etc.	♂ 3 cm. × 0.6 ♀ 70 cm. × 1.1 mm.	Subcutaneous tissue.
	Sexually immature. Imperfectly known.	Agamofilaria.	*A. georgiana.*		Subcutaneous tissue.
			A. oculi.	6.5 mm.	Eye.
			A. palpebralis.		Eye.
VIII. *Mermithidæ:* Intestinal canal incomplete; anus absent.	Sexually mature. Parasites in the body of insects. Body very slender (called "hair worms").	Mermis.	(?)		
	Sexually immature. Occasionally parasites of man. Imperfectly known.	Agamomermis.	*A. restiformis.*	50 cm. × 0.5 mm.	Urethra. (?)

Subgenus: *Agamofilaria* (Stiles, 1906).—A collective group of sexually immature Filaridæ, imperfectly understood.

Species: *Agamofilaria georgiana; A. oculi; A. palpebralis.*

Family VIII. Mermithidæ.—Nematodes with six mouth papillæ and without anus. Male with two spicules and three rows of numerous papillæ.

Genus: Mermis, with the characteristics of the family.

Subgenus: Agamomermis.—A collective group of sexually immature Mermithidæ, imperfectly understood.

Species: *Agamomermis restijormis* (Leidy, 1880); *Filaria* (?) *hominus oris* (Leidy, 1850).

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CHAPTER XVIII

ORDER III. NEMATODA (Continued)

THE PARASITIC NEMATODES OF MAN

Nematodes of the Intestine.—Nematodes of the Lymphatics and Blood.—Nematodes of the Subcutaneous Tissues.—Nematodes of the Kidneys.—Nematodes of the Lungs.—Erratic Nematodes.

In order to facilitate the clinical study of the parasitic nematodes of man, they will be divided as was done in the case of the trematodes and cestodes, according to their most common habitat in the body, into the following groups: I. Nematodes of the intestine; II. Nematodes of the lymphatics and blood; III. Nematodes of the subcutaneous tissues; IV. Nematodes of the kidneys; V. Nematodes of the lungs; VI. Erratic Nematodes. It may be observed here that the parasites of the intestine are the most important of these, since they represent more than 50 per cent. of all infestations; about 20 per cent. parasitize the subcutaneous tissue, lymphatics, and blood, and only a small number are found in other parts of the body.

I. NEMATODES OF THE INTESTINE

FAMILY ASCARIDÆ

1. **Ascaris lumbricoides** (Linnæus, 1758).—This parasite is the largest of all the nematodes of the intestine. It is pointed at both ends, and whitish yellow in color, with often a slightly reddish tinge. The *male* measures 15 to 20 cm. in length by 3 mm. in diameter. The caudal extremity is conic, curved ventrally, and provided with two spicules, 2 mm. in length. The cloaca is subterminal, and on each side of it are from 70 to 75 small papillæ, of which seven pairs are post-anal. The *female* is about twice as large as the male. It measures 20 to 40 cm. in length by 5 mm. in breadth. The tail in both sexes is slightly pointed. The head is small and provided with three lips—one dorsal and two ventral. The edges of the lips are serrated and contain, in addition, four papillæ—two for the dorsal and one for each of the ventral lips. The vulva in the female is situated at the junction of the anterior and middle thirds of the body.

Habitat.—The parasite usually inhabits the lower part of the small intestine. It is one of the most common intestinal parasites in the tropics. It is frequent in children under ten years of age, and more especially between the second and sixth years, but is sometimes

found also in adults. At postmortem examination the worm may be found in any part of the gastro-intestinal tract, in the peritoneum, the larynx, trachea, or bronchi. In rare instances it has also been found in the bile and pancreatic ducts, in the appendix, in abscesses of the body wall, and in the liver.

Life History.—The eggs are deposited in the intestine, and as found in the feces they usually appear unsegmented, oval in shape,

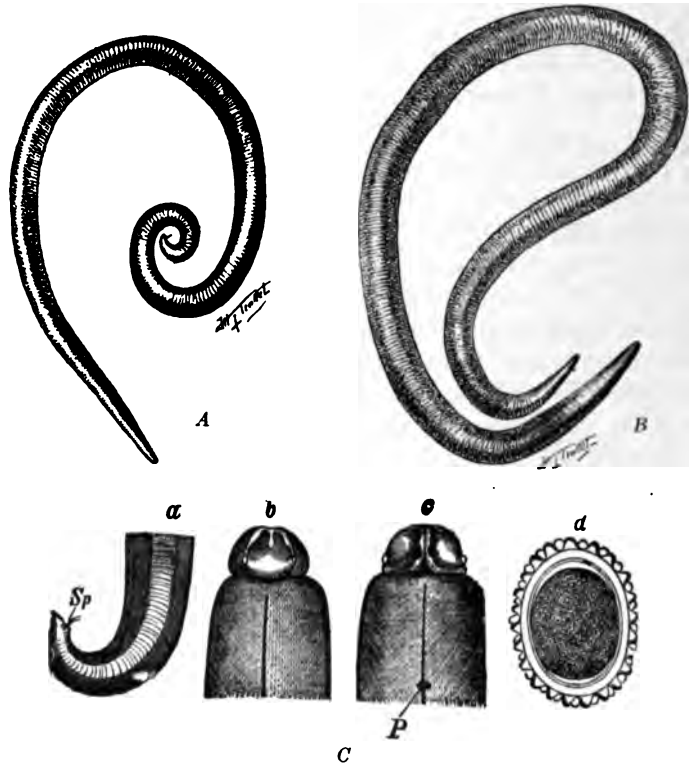


FIG. 175.—Ascaris humbricoides. *A*, adult male and *B*, adult female, natural size. (*After Brumpt.*) C, Cephalic, caudal extremities and egg. (*After Leuckart in Brumpt.*) *a*, Caudal extremity showing the spicules (*Sp*); *b* and *c*, dorsal and ventral view, respectively, of cephalic extremity; *d*, egg.

thick shelled, measuring 50 to 70μ by 40 to 50μ, and provided with a delicate albuminous membrane or coating that gives the egg an irregular outline. Under suitable conditions of moisture and temperature, the egg deposited in the soil or water gives rise to an embryo in about thirty to forty days, which does not hatch, however, until it enters the body of man or other susceptible host (Davaine, Grassi, Calandruccio, Lutz, etc.). On reaching the intestine the larva is set free and attains the adult stage in about five to six weeks.

The researches of F. H. Stewart seem to prove that the life

history of *Ascaris lumbricoides* requires an intermediate host—the rat, *Mus decumanus*, or the mouse, *Mus musculus*. The mature egg, on being swallowed, hatches a larva in the alimentary canal of these rodents, and then passes to the lung, where it undergoes developmental changes. The manner in which the larva is transmitted to the primary host has not been demonstrated. In the embryonic stage, inclosed in the egg-shell, it may remain alive for a long time (five years in water, Davaine). It withstands a freezing temperature and also 42° C. for some time. The duration of life of *Ascaris lumbricoides* is not known, but is probably about three to five years.

Mechanism of Transmission.—Man is infested through drinking polluted water, eating contaminated fruits and vegetables, by soiled fingers, etc. The common habit, among the poorer classes in certain tropical countries, of permitting children to play on the ground is the most common source of infestation.

Pathogenesis.—The presence of a few parasites in the intestine may not give rise to any appreciable symptoms, except in those in-

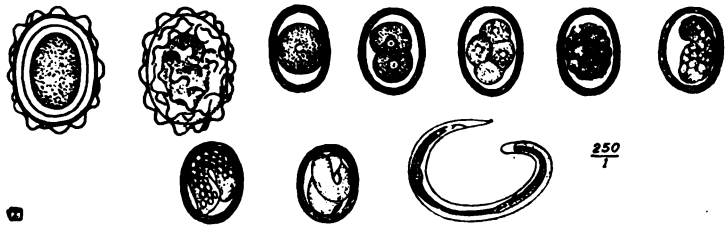


FIG. 176.—Development of Ascaris lumbricoides. (*After Stiles in Castellani and Chalmers.*)

stances in which the worms invade the pancreatic or bile duct or the appendix. The most common symptom in marked infection is gastro-intestinal disturbance, which may be manifested in the form of diarrhea with occasional bloody stools, alternating with constipation. Nausea and periodic attacks of colic, without any appreciable rise in temperature, are of common occurrence. Nervous and toxic symptoms, such as convulsions, nightmare, mental and physical weakness, idiocy, perversion of appetite and of sensation, pruritis (anal and nasal), hemiopia, photophobia, etc., are not infrequent.

Diagnosis.—The diagnosis is made by finding the eggs in the feces; these are, as a rule, very abundant. A small portion of the feces is softened and suspended in a little water, applied to a cover-glass, and examined with the microscope. The identification of the eggs offers no difficulty. They are thick shelled, usually contain a single cell, and measure from 50 to 70μ by 40 to 50μ.

When, for obvious reasons, a microscopic examination of the feces cannot be made, I have observed that gentle palpation and massage

of the abdomen will often reveal the presence of an irregular nodular tumor, made up of several ascarides coiled together, which, on further manipulation, disappear, to be reformed again in other portions of the intestine.

Prognosis.—The prognosis of ascariasis is, as a rule, favorable, except when the condition is associated with grave complications, such as obstruction of the pancreatic or bile ducts, etc.

Treatment.—Santonin, in doses of from one-half to one grain in castor oil, is almost specific. The drug should be taken in the morning, on an empty stomach, and no food should be eaten for from two to four hours. After this time it is best to administer a purgative, preferably castor oil, and keep the patient on a light diet during the remainder of the day.

2. **Ascaris (?) texana** (Smith and Goeth, 1904).—This worm was found by Smith and Goeth in Texas. Only the female is known. It measures 58 to 60 mm. in length by 1 to 1.5 mm. in width. The uterine eggs measure 60μ by 40μ. This nematode appears to be a very rare parasite of man.

3. **Ascaris (?) maritima** (Leuckart, 1876).—This worm was vomited by a child. The parasite was probably an immature female ascaris, common in the lower animals, and perhaps accidentally swallowed with the food.

4. **Belascaris mystax** (Zeder, 1800).—This parasite is commonly found in the intestine of cats and occasionally in man, in whom it rarely gives rise to appreciable symptoms. The head of the adult worm is curved ventrally, and is provided with two lateral expansions, which causes the parasite to resemble in appearance the point of an arrow. The male measures 4 to 6 cm., and the female, 4 to 10 cm. in length. The eggs are globular, and from 65 to 80μ in diameter. The life history is not sufficiently understood, but is probably similar to that of *Ascaris lumbricoides*.

5. **Toxascaris canis** (Werner, 1782).—This parasite, also known as *Ascaris canis*, is the common round worm of the dog. Leiper found it once in man in Egypt. This worm and *Belascaris mystax* of the cat were at one time regarded as identical, but Leiper found them to be of different species. The two parasites are very similar, but are differentiated from each other by the curving of the head dorsally in *Toxascaris canis*, instead of ventrally, as in the case of *Belascaris mystax*. The former is also slightly larger than the latter. The male measures 5 to 10 cm. and the female 9 to 12 cm. in length. The eggs are globular and from 75 to 80μ, in diameter. The life history is not well understood. Development is probably direct.

6. **Oxyuris vermicularis** (Linnæus, 1767).—This parasite, commonly known as the "pin" or "seat" worm, is a small nematode,

characterized by the presence of two cuticular ridges along the ventral and dorsal surface of the body. In the female these ridges unite posteriorly to form a tail-like appendage that projects beyond the body proper for about one-fourth the entire length of the parasite. The *male* measures 3 to 5 mm. in length. The posterior end is rolled spirally ventrally and provided with a single spicule and six papillæ. The *female* is about 10 mm. in length by 0.6 mm. in breadth. The eggs are bean shaped, flattened on one side, and measuring 50 to 52μ by 16 to 24μ. As discharged from the uterus and found in the feces they are thin shelled and commonly contain a fairly well-developed embryo.



FIG. 177.—Oxyuris vermicularis. The male is to the left, the female to the right. (*After Claus in Castellani and Chalmers.*)

Habitat.—It is believed that this worm when young, inhabits the lower part of the small intestine, and that, after fertilization, the male dies and the adult female travels to the cecum and colon. It has a great tendency to migrate through the anus to the exterior of the body. In women they may invade the vagina, thus explaining the symptoms of pruritus and nymphomania not uncommonly encountered. The parasite may also invade the appendix, and give rise to appendicitis. *Oxyuris vermicularis* is a cosmopolitan parasite, known from earliest times, and, so far as is known, found only in man.

Life History.—The embryo eggs, as discharged with the feces, are reintroduced into the mouth directly, as by soiled fingers, or through the medium of contaminated vegetables, fruits, etc. On reaching the intestine the eggs hatch and develop into male and female parasites. After fertilization the males die and the females wander to the large intestine, where the eggs are discharged with the feces and the cycle is repeated.

The duration of life of *Oxyuris vermicularis* in man is not known, but probably does not exceed two to three years.

Mechanism of Transmission.—Transmission of the parasite is direct, and takes place chiefly through contamination of the fingers, fruit, or vegetables, etc., with the eggs of the worm. The infective stage in the life history is represented by the embryo egg, as found in the feces, and this explains why autoinfection and subsequent reinfections with Oxyuris are common. Infestation may also take place indirectly through contaminated water, but this is apparently of secondary importance, as the life of the embryo in the outer world

is comparatively short. Autoinfection is very common, particularly in children. The pruritus caused by the parasite facilitates the conveyance of the eggs from the anus by means of the fingers or nails

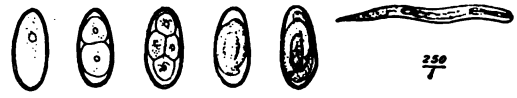


FIG. 178.—Development of Oxyuris vermicularis. (*After Leuckart, from Stiles.*)

during the act of scratching, and thus explains the intensity of the infestation observed in some cases, and also the infection of several members of the same family. Parents may become infested by attending to the toilet of their children, and children may become contaminated by the soiled hands of adults.

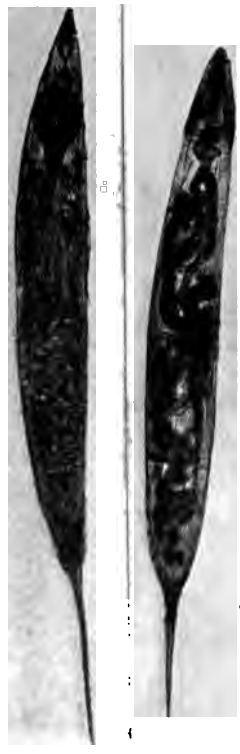


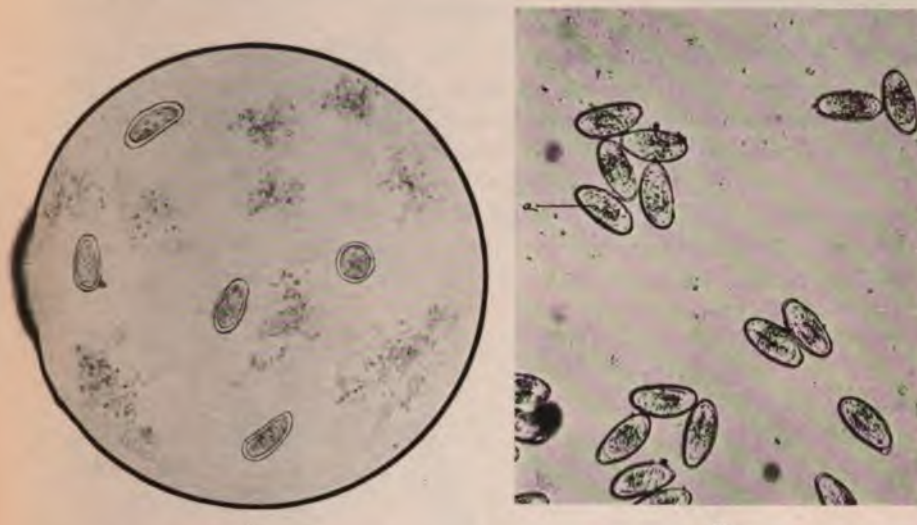
FIG. 179.—Female oxyures from cloaca of cockroach (*Periplaneta orientalis*). Oxyuris diesingi to the left and Oxyuris appendiculata to the right. Each under same magnification.

Pathogenesis.—The presence of *Oxyuris vermicularis* in man is the cause of a variety of more or less intense symptoms, depending upon the degree of infestation. When the worms are present in large numbers, they may give rise to a marked enterocolitis. One of the most constant symptoms is the pruritus, which appears with remarkable periodicity at bedtime. The parasite may also be the cause of appendicitis and nervous derangements, particularly in children; these give rise to convulsions, vertigo, urinary incontinence, etc. The irritation of the anus produced by the worm may directly or indirectly lead to derangement of the genital organs, and give rise to erections, erotic dreams, spermatorrhea, onanism, nymphomania, dysmenorrhea, etc.

Diagnosis.—The variety of symptoms in oxyuriasis renders the diagnosis somewhat difficult. The pruritus and a certain degree of eosinophilia should be regarded with suspicion. The diagnosis is made by finding the adult female around the anus or from the presence of eggs in the feces or urine.

Treatment.—The adult females are dislodged from the rectum and anus without difficulty by rectal injections of soapsuds, salt solution, tannic acid, or a 1 per cent. infusion of santonin. For the removal of the young parasites which inhabit the small intestine, internal medication should be employed, such as thymol or santonin. It

is most important to prevent autoinfection, and this is best accomplished by proper cleansing of the hands of the patient and by allaying the pruritus by local medication applied to the anus and perineum.



A B

FIG. 180.—Ova of oxyuris vermicularis. *A*, in the feces. *B*, preparation from adult female. Note asymmetry of (*a*).

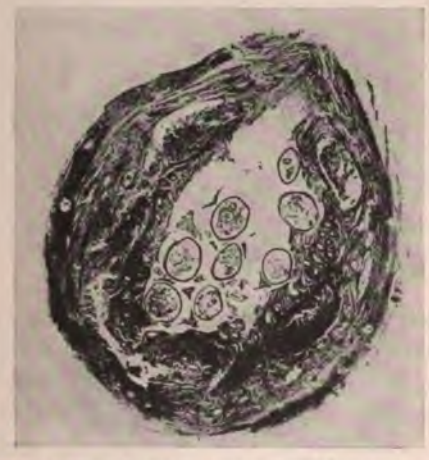


FIG. 181.—Transverse section of inflamed appendix showing Oxyuris vermicularis in lumen.

The wearing of pajamas at night will prevent contamination of the patient's fingers during sleep.

Prophylaxis.—Prophylaxis includes: (1) The avoidance of the use of human excrement as fertilizer; (2) disinfecting the clothes of the

patient by boiling; (3) avoiding autoinfection by proper cleansing and disinfection of the hands; (4) the use of filtered water and the thorough washing of vegetables, legumes, and fruits that are used as food.

FAMILY STRONGYLIDÆ

1. **Ankylostoma duodenale** (Dubini, 1843). *History.*—Although it is probable that this worm was known to the ancient Egyptians under the name "Heltu," mentioned in the Ebers Papyrus, about 1550 B. C., it was not until 1838, when Dubini discovered the parasite in Italy, that modern medicine obtained definite knowledge of its occurrence in man. The findings of Dubini were corroborated by Pruner in 1846, by Griesinger in 1851 in Egypt, and by Wucherer in 1871 in Brazil, the latter showing that it was the cause of Egyptian

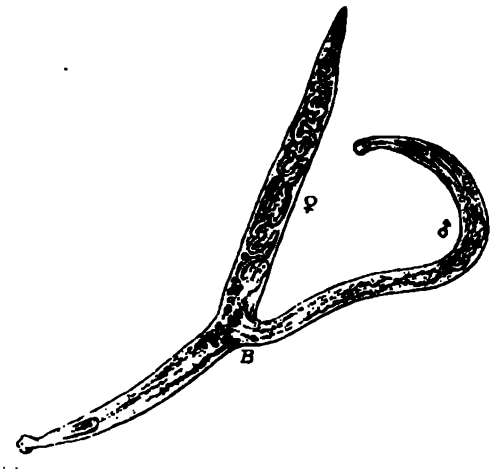


FIG. 182.—Ankylostoma duodenalis in copulation. The male, ♂, is attached to the female, ♀, by means of the bursa copulatrix, *B*.

and of tropical anemia respectively. In 1878 Grassi found the eggs in the feces. The life cycle of the parasite was worked out by Looss in Egypt, and in 1902 Stiles differentiated *Ankylostoma duodenale* from *Necator americanus*. In recent years the wide geographic distribution of the parasite has been recognized, and also the large variety of diseases, such as anemias, dropsy, a certain form of beriberi, etc., which are caused by this worm.

Description.—The worm is cylindric, somewhat pointed at both ends, and pale reddish in color when alive. The mouth is terminal, and the anterior end bent dorsally. The buccal cavity is lined by a chitinous wall; it has an anterior and a posterior lip, and is armed with

two pairs of ventral hooks, on each side of the midline, and a single dorsal tooth, small in size. Closely applied about the midline there is a pair of chitinous pharyngeal plates or lancets in the floor of the buccal cavity, situated latero-ventrally, one at each side and close to the



FIG. 183.—Buccal cavity and mouth of old world hookworm (*Ankylostomum*) *A* and American hookworm (*Necator*) *B*, showing teeth or hooks in former and cutting ridges in latter. *A*, × 100; *B*, × 230. (*After Looss in Chandler.*)

base of the outer ventral hook. The buccal cavity, therefore, contains seven cuticular appendages, namely: four hooks, one tooth, and two plates, which serve as organs of attachment by means of which the parasite fastens itself to the intestinal mucosa of the host.



FIG. 184.—Head of Ankylostoma canina of dog.

The worm is provided with a pair of unicellular glands—the *head* or *cephalic glands*—which extend through the length of the esophagus and open at the base of the anterior ventral hook. These glands secrete a substance that, as found by Loeb and Smith, prevents the

coagulation of the blood. In addition the parasite also has a pair of cervical glands, the ducts of which open into the excretory pore. Finally, the male is provided with a pair of anal glands that empty into the cloaca.

The *male* (Fig. 185) is about 10 mm. in length by 0.4 to 0.5 mm. in breadth. The posterior end is provided with a fan-shaped bursa copulatrix, supported by eleven chitinous bands or ribs (Fig. 186) arranged as follows: (1) One dorsal rib, which divides near the margin of the bursa into two branches, each of which subdivides into three small lobes; (2) one pair of dorsolateral ribs; (3) two pairs of lateral ribs; (4) one pair of ventrolateral ribs; (5) one pair of ventral ribs, one on each side, the latter divided at the extreme end into two small lobes. The order and number of ribs are, therefore, one dorsal, two dorsolateral, four lateral, two ventrolateral, and two ventral, so arranged as to divide the bursa into three lobes: one dorsal, made by the dorsal rib, and two lateral lobes, made by the dorsolateral, lateral, ventrolateral, and ventral ribs on each side. Near the center of the bursa is a small spicular sac, at the base of which is the cloacal opening, and through which project two slender spicules, each about 2 mm. in length. The other parts of the male reproductive organs consist of



FIG. 185.

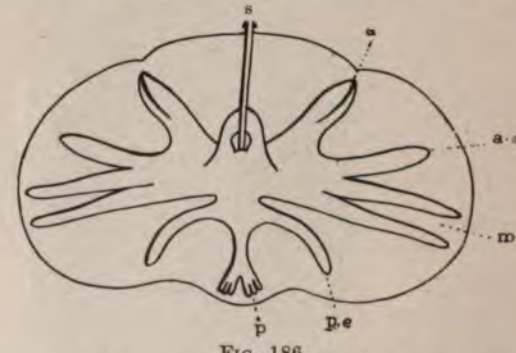


FIG. 186.

FIG. 185.—Agchylostoma duodenale dubini (male). (*After Looss in Castellani and Chalmers.*)

FIG. 186.—Ankylostoma duodenalis, bursa copulatrix of the male. *s*, Spicules; *a*, anterior ribs; *ae*, antero-external (lateral) rib; *m*, medial (lateral) ribs; *pe*, postero-external (lateral) rib; *p*, posterior rib. (*After Railliet in Brumpt.*)

tubular testes, vesicula seminalis, and a long cement gland whose secretion fixes the male to the female during copulation.

The *female* measures 12 to 13 mm. in length and 0.7 to 1 mm. in width. The reproductive organs consist of two elongated ovaries, receptaculum seminis, and uterus, which unite to form a short vagina.

The vaginal opening is at the junction of the middle and posterior third of the body. The end of the tail is slightly pointed, conic in shape, and has no bursa.

Habitat.—The common habitat of the adult parasite is the duodenum and upper part of the small intestine of man, but the worm has also been found in the appendix. It may likewise inhabit the small intestine of anthropoid apes. Experimentally it may develop for a certain time in the small intestine of young cats (Looss). In the free larval stage it may live for some time—about two weeks or a month—in the soil.

Life History.—Cleavage begins in the uterus and alimentary canal of the host. The eggs, as discharged with the feces are commonly found in the four-cell stage. On the outside, under proper conditions of temperature (25° to 30° C.), water, oxygen, and darkness, it develops in about twenty-four hours into an embryo, which can be seen coiled up in the egg; from this it escapes as a larva. The larva is needle shaped, pointed posteriorly, *rhabditiform* (bulbed esophagus), and measures from 200 to 250μ in length by 15 to 17μ in breadth. It has a complete alimentary canal, with the mouth terminal and the anus at some distance from the tip of the tail (Fig. 189). It feeds on fecal material.

At this early stage the larva is very active. It now grows rapidly, and after three days measures about 300μ. About the fifth day the *first molting* takes place, and the shape of the esophagus changes: it becomes cylindric, the bulb disappears, and the larva takes on the *strongyloid* or filiform appearance. At this

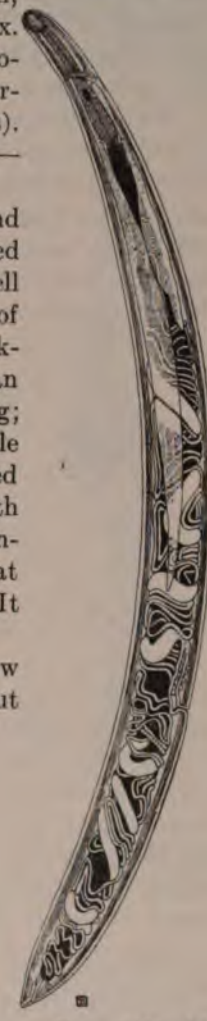


FIG. 188.—Agchylostoma duodenale dubini (female). (*After Looss in Castellani and Chalmers.*)



FIG. 187.—Bursa of Uncinaria canina.

stage the gonads begin to appear, and the larva becomes encysted by the formation of a new skin inside of the cuticle; it measures 560 by 24μ, ceases to grow and to feed, and may remain dormant for a month. It is now ready to infect man, which it accomplishes by penetrating the hair-follicles of the skin, causing an eruption or sores known as "ground itch," "coolie itch," "sore feet," "bunches," "mazamorra," etc. The larva may also be swallowed with contaminated food, water, etc., or be directly carried to the mouth by soiled fingers.

While penetrating the skin the larva molts again (*second molting*), and then, on entering the lymphatics or venous blood, it reaches the right heart and the capillaries of the lungs. It now works its way into the air-sacs, and travels up the bronchi, trachea, larynx, and esophagus, and is carried with the food to the stomach and intestine. The time occupied by this journey is from seven to ten days, during which the larva molts again (*third molting*), on the seventh day, this occur-

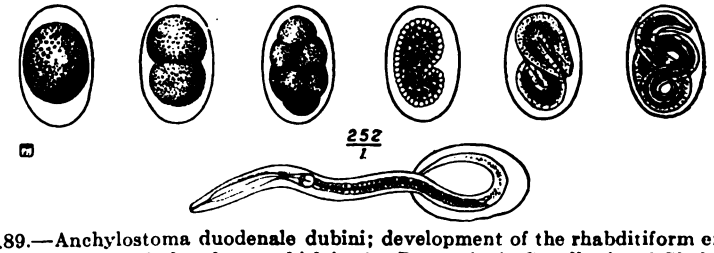


FIG. 189.—Anchylostoma duodenale dubini; development of the rhabditiform embryo (*After Looss, except the last figure, which is after Perroncito in Castellani and Chalmers.*)

ring either in the lungs or in the stomach, as the case may be. A temporary buccal capsule is formed, provided with a dorsal and a ventral pair of teeth. At this stage the sexual organs are further developed, and the larva passes to the intestines. Here it continues to grow, and the permanent buccal capsule begins to appear. The sexual organs are differentiated, and the *fourth molting* takes place about the thirteenth day. The larva now measures 3 to 5 mm. in length by 120 to 140μ in width.

After three weeks the young worm begins to attain maturity, and by the fourth week copulation takes place, the eggs being discharged about the seventh or eighth week, after which the cycle is repeated. The life history of *Ankylostoma duodenale* may, therefore, be divided into seven stages (Fig. 190) as follows:

First Stage.—From the fertilization of the egg to the hatching of a rhabditiform larva—twenty-four to forty-eight hours.

Second Stage.—Free larval stage of development in the soil, transformation of the rhabditiform into filiform or strongyloid larva, and occurrence of first molting—about three days.

Third Stage.—This is the encysted or resting stage, in which the larva forms a new skin within the chitinous cuticle in about two days. In this condition the larva may remain unchanged for months, and represents the infective stage of the parasite.

Fourth Stage.—Entrance of the larva into the host, either through the skin or by the mouth, and occurrence of the second molting.

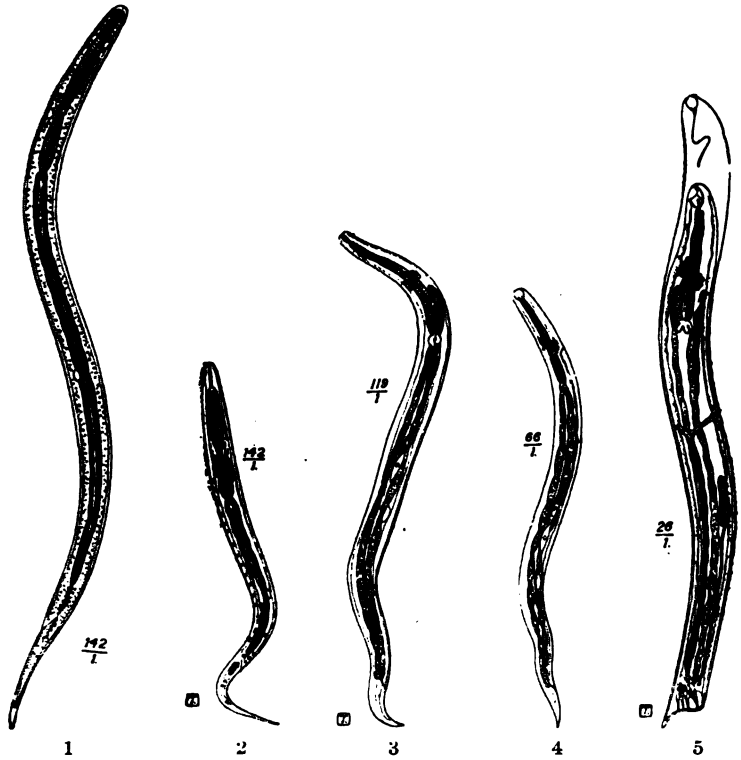


FIG. 190.—Development of the larva of Ankylostoma duodenale. 1. First (larval) stage of development. (*After Looss, from Mense.*) 2. Second stage of development. (*After Looss, from Mense.*) 3. Third stage of development. (*After Looss from Stiles.*) 4. Fourth stage of development. (*After Looss, from Stiles.*) 5. Fifth stage of development. (*After Looss, from Stiles, in Castellani and Chalmers.*)

Fifth Stage.—Formation of a temporary buccal capsule with two pairs of teeth, beginning development of genital organs, and occurrence of third molting, which may occur either in the lungs or in the stomach, as the case may be.

Sixth Stage.—Development of permanent buccal capsule, differentiation of genital organs, and fourth molting in the intestine—about seven days.

Seventh Stage.—The young worm grows to adult size, and copulation takes place in about one week. The eggs are found in the feces of

the host at about the seventh or eighth week after the entrance of the larva in the body.

From the foregoing it may be seen that the development of ***Ankylostoma duodenale*** is direct—that is, it takes place without an intermediate host; that the complete cycle may take place in about four weeks, and that it consists of two stages: one outside (free larval stage) and the other in the host. The former occupies from three to five days, during which the parasite undergoes developmental changes preparatory to effecting an entrance into the host, and the latter occupies about three weeks, during which it grows to adolescence. In all, four moltings take place—the first two outside (during the free larval stage) and the other two within the host; the third occurs in the respiratory organs or in the stomach, and the fourth in the intestine, when the

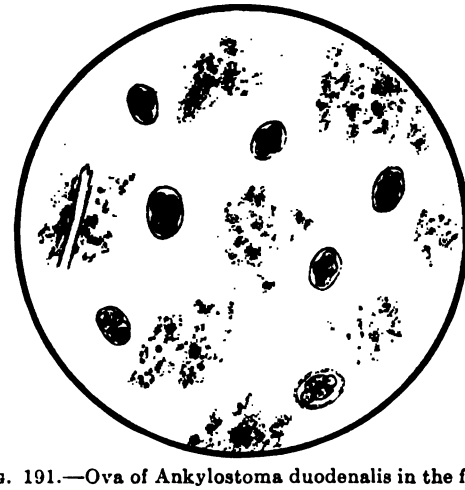


FIG. 191.—Ova of Ankylostoma duodenalis in the feces.

larva enters through the skin. If, however, the larva enters the host through the mouth, only the first molting takes place outside and the others occur in the stomach and intestine.

Mechanism of Transmission.—The infective stage in the life history of *Ankylostoma duodenale* is represented by the free filiform encysted larval stage, which corresponds to the third stage just described. The larvæ gain entrance into man through the hair-follicles of the skin (Fig. 193) and traveling via the subcutaneous tissues (Fig. 194) into the venous blood and lymphatics, reach the heart and lungs. From the capillaries of the lungs, by traversing the walls of the air-cells, they pass into the bronchi, trachea, larynx, esophagus, and stomach, and attach themselves to the mucosa of the intestine, where they develop into adult worms. The time occupied between the entrance of the larvæ through the skin and the discharge of eggs by the adult female

is from four to six weeks, and eggs may be found in the feces after seven weeks (Smith).

According to Sambon, the larva may pass from the pulmonary artery to the pulmonary vein and the left heart, from which it is carried by the blood stream to the duodenum and jejunum, the mucosa of which it pierces and enters the lumen of the intestine.

The larva may also gain entrance through the mouth, through the medium of contaminated water, food, soiled fingers, etc. Since the discovery by Looss, of the entrance of the larva through the skin, infection through the mouth has been considered of secondary importance, but it is probable that this mode of transmission of the parasite is more common than is generally believed (Stiles).

Pathogenesis.—The parasite inhabits the duodenum and jejunum, but in very marked cases of infestation it may also be found in the ileum. The presence of the parasite in man gives rise to certain mor-



FIG. 192.—Transverse section of intestine of dog showing a healed ulcer of duodenum at site of Uncinaria attachment.

bid conditions, brought on by the ulceration of the intestinal mucosa, the possible absorption of toxic substances, the mechanical action of the parasite upon the intestine, secondary bacterial infection, etc. This condition is known as ankylostomiasis. The disease manifests itself by a variety of symptoms, such as gastro-intestinal derangement, gastric pains, anorexia, bulimia, perversion of appetite, pica, or geophagia. The last-named symptom, which is common in some countries, is the cause, rather than the effect, of the disease (Brumpt). Nausea and occasional vomiting, diarrhea alternating with constipation, dysentery, distention of the abdomen, irregular fever, skin eruptions, and physical and mental lethargy are common symptoms. Circulatory disturbances, such as palpitation, edema of the lower extremities, ascites, anemia, etc., and nervous disturbances, such as vertigo, are not uncommon. Emaciation and cachexia may occur in the latter part of the disease and in fatal cases. Death is usually due to a profound anemia, marasmus, or septicemia, which is intestinal in origin, the

bacteria gaining entrance into the body through the ulcerated surface of the intestine.

Of all the symptoms enumerated, a secondary anemia, more or less profound and pernicious in type, is very common, and when associated with a certain degree of eosinophilia, it should be regarded with suspicion. The hook-worm was long believed to feed entirely on blood, but the work of Looss on *A. duodenale*, and that of the Porto Rico American Hook-worm Commission, have demonstrated that the parasite derives its nourishment from the mucosa of the intestine. The researches of Leo Loeb and Allen J. Smith demonstrated that the secretion of the worm, probably coming from the cephalic glands, contains a substance, an anticoagulant, that is comparable to the "hirudine" extract obtained from the head of leeches. This substance, by preventing coagulation of the blood that flows from the ulcers of



FIG. 193.—Larva of Ankylostoma duodenalis in the hair follicle of experimental dog.

the intestine, favors constant bleeding from this area, and thus accounts for the anemia.

Morbid Anatomy.—The lesions commonly seen in ankylostomiasis are: (1) Alterations in the blood; (2) changes in the internal organs; and (3) pathologic changes in the digestive tract.

(1) *Alterations in the Blood.*—The anemia is more or less profound and pernicious in type, especially in advanced cases. The hemoglobin may be diminished to 30 or even to 17 per cent.; the erythrocytes may fall from 3,000,000 to 1,000,000 or less. A certain degree of leukocytosis, due probably to a latent and chronic bacterial infection, is not uncommon, but the poikilocytosis common in idiopathic pernicious anemia is usually absent. At times, due either to a mild infestation or to a marked resistance of the organisms, the blood may show merely a moderate degree of anemia and eosinophilia.

(2) *Changes in the Internal Organs.*—At autopsy the body, as a rule, does not appear to be emaciated. Edema is not uncommon. The organs are pale and anemic. The heart, kidneys, and liver are the seat of cloudy swelling and fatty degeneration. A serous exudate may be present in the peritoneum, pericardium, and pleura. The meninges and the substance of the brain may be the seat of small and numerous hemorrhages, especially at the corpus callosum. The bone-marrow is red and gelatinous.

(3) *Pathologic Changes in the Digestive Tract.*—The duodenum, jejunum, and sometimes the ileum, are the seat of numerous and small ulcerations (Fig. 192) surrounded by an ecchymotic area. If the autopsy is made within three hours after death occurs, the parasites may still be found attached to the intestinal mucosa, near to, or at the points

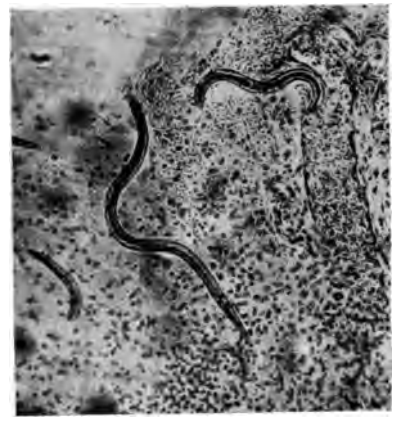


FIG. 194.—Larvæ of Ankylostoma duodenale in subcutaneous tissue of experimental dog.

of, the ulcers. Twenty-four hours after death has occurred the worms are found detached and mixed with the intestinal contents, which usually contains blood. Not uncommonly pigmented points, the cicatrices of previous ulcerations, may be seen.

Diagnosis.—In the tropics, where ankylostomiasis is frequent, the diagnosis may be made without difficulty; care should be taken, however, to differentiate this disease from malarial cachexia, beri-beri, sleeping sickness, and other chronic affections, such as tuberculosis, etc., with which it may be confounded. The fact that there is no loss of weight in ankylostomiasis is a valuable point in the differentiation between this disease and tuberculosis and cancer. As a rule, a certain degree of anemia and eosinophilia, when associated with gastro-intestinal disturbances and edema, should be regarded as suspicious; but the diagnosis can be made with certainty only by examining the feces.

The feces should be examined for the presence of occult blood and the eggs of the parasite.

Test for Occult Blood.—For the detection of occult blood the benzidin test is to be recommended. This is made as follows:

1. Soften a small portion of the feces, if necessary, with water, and add a few cubic centimeters of glacial acetic acid.

2. Mix thoroughly by stirring with a clean glass rod; then shake the mixture forcibly with about an equal volume of ether. Let it stand for a few minutes and decant the ether. The hematin which may be present in the feces is dissolved in the ether.

3. In a clean porcelain dish or a test-tube dissolve a few grains of benzidin in a little glacial acetic acid, and add a few cubic centimeters of fresh hydrogen dioxid.

4. Add the ethereal extract to the dish or test-tube. The appearance of a distinct green or darkish tint at the line of contact of the two liquids shortly after the addition of the ethereal extract indicates the presence of blood in the feces. On permitting the liquid to stand for five minutes or longer it will be noticed that it takes on a light greenish or darkish tint, which should not be mistaken for a positive reaction, as this reaction is seen in normal feces.

Another important precaution that should be taken is to be sure that the hydrogen dioxid used is fresh. To avoid error, especially when the reaction happens to be negative, make a duplicate test with the ethereal extract of feces, to which a few drops of blood have previously been added as control.

Search for the Eggs.—The feces are examined for the eggs of the parasite by making a fresh cover-glass preparation of the material, and looking for them under the low power of the microscope. The feces may also be softened in water, if required, suspended in an excess of water, centrifuged, and preparations made from the sediment. The eggs of Ankylostoma are easily recognized: they are oval in shape, thin shelled, and light in color or colorless. They measure about 60μ by 40μ. They are so abundant that in some cases as many as 20,000 per gram of feces may be counted (Leichtenstern). It has been estimated that from 15 to 18 eggs per gram of feces corresponds to a single female and male parasite.

Treatment.—The drug most commonly used is thymol. (See Chapter XVII, page 357.) This drug may also be given in the form of thymotal, an odorless and tasteless preparation, in doses of 15 gr. three or four times daily for four consecutive days, followed by a purgative. Betanaphthol, administered in the same way as thymol, etc., is also recommended. Essence of eucalyptus has proved useful, and may be given according to the following formula:

Essence of eucalyptus	20–30 drops
Chloroform	1 dram
Castor oil	1½ ounces

This should be taken on an empty stomach, in the morning, and be given in two doses, at intervals of half an hour. If necessary, this treatment should be repeated for several consecutive days.

No treatment should be regarded as successful until, after repeated examinations for weeks or months, the eggs of Ankylostoma are no longer found in the feces. Convalescence should be hastened by careful diet and the administration of iron and arsenic.

Prophylaxis.—Our present knowledge of the life history of Ankylostoma enables the hygienist to formulate certain prophylactic regulations that, if carefully followed, will result in the prevention of ankylostomiasis. Knowing that, under favorable conditions of temperature (about 27° C.), an egg of the parasite may develop into a strongyloid larva in about five or six days, that this larva, either by penetrating the skin (in four to eight minutes), or by entering through the mouth, reaches the intestine, attains maturity in about four weeks, and the eggs may be found in the feces after seven or eight weeks; that these eggs in turn give rise to new larvæ in the soil and may infect others; that as these larvæ are very resistant to dryness, antiseptic measures, etc., they may remain alive for months, and consequently can be carried to distant places with the clothes, or may be washed away by the rain and develop new foci of infection in other localities. Finally, that the breeding place for the larvæ are the mines where the three conditions, moisture, temperature, and darkness, are most favorable for their development, and that an infected person is a constant menace to others.

With these points in mind, the prophylactic treatment of ankylostomasis may be summarized as follows:

1. *Treatment of Infected Individuals.*—A thorough examination should be made of workers in mines and of suspected persons in places where ankylostomiasis is prevalent. All cases in which eggs are found in the feces, whether or not the person presents any symptoms of the disease, should be treated. The infected individual should be isolated during the treatment, and should not be permitted to associate with others until after several examinations, made at intervals of days or weeks, show that eggs are no longer present in the excrement.

2. *Disinfection of Excrement.*—The feces should be disinfected with chlorid of lime or carbolic acid, or, better, they should be burned or buried deep in the ground. They should never, however, be used as fertilizer.

3. *Sanitation of Mines.*—A 5 per cent. solution of lysol, chlorid of lime, or sulphate of iron should be applied to the ground, and also

used as a spray on the walls of the mines. It has been observed that in certain mines the decomposition of iron bisulphate into iron sulphate and sulphuric acid gives rise to a sufficient degree of acidity in the water to prevent the development of the larvæ. In others, natural infiltration with salt acts in the same way. As a certain degree of humidity and temperature is essential for the development of the larvæ, proper ventilation of the mines will effect both dryness and lowering of the temperature.

4. *Change of Clothing.*—As has previously been stated, the strongyloid larva lies dormant for days or weeks, resists dryness for some time, and may be conveyed to man with the clothes, untensils, etc. In view of this fact, therefore, it should be made compulsory for mine laborers to use special clothing for their work, and to change these clothes before going to their homes. If possible, a bath should be taken, but if this is not practicable, the hands, face, and other exposed parts of the body should at least be washed. The washing of the hands in particular and the use of an antiseptic should receive careful attention.

5. *Education of the Public.*—The education of the public is undoubtedly the most important step in the prophylactic treatment of ankylostomiasis. Most of the prophylactic measures described are bound to meet with only partial success if the laborer in particular, and the community at large, are not instructed concerning the danger of the disease. The education of the public should be carried out by means of lectures, conferences, the posting of appropriate notices in the mines, and all other possible means of explaining how the disease can be controlled, its gravity and the means for its prevention. Especial emphasis should be laid on the fact that every carrier of the parasite is a danger to himself, to his companions in the mine, to his family at home, and to the community in general. The need for receiving proper treatment should also be impressed upon the patient.

2. **Ankylostoma ceylanicum** (Looss, 1911).—This hook-worm, commonly found in cats in Ceylon, may, according to Clayton-Lane, be found in man in Bengal. A characteristic of this parasite is that it has a pair of large conic teeth at the anterior edge of the buccal capsule, and below, or behind them, toward the median line, another pair of small teeth, only the tips of which are seen. The male measures about 5 mm. and the female about 7 mm. The bursa in the male is almost as long as it is broad, and the ribs are short and relatively thick.

3. **Necator americanus** (Stiles, 1902).—This species bears so close a resemblance to *Ankylostoma duodenale* that, to the naked eye, it is almost impossible to differentiate one from the other. For a long

time both were described under the head of Ankylostoma until Stiles, in 1902, observed the difference and called the new genus Necator.

Allen J. Smith saw the ova of the parasite in the feces of a man in Galveston, Texas, and also recognized a difference between this worm (expelled by the patient) and *Ankylostoma duodenale*, but believed it to be *Uncinaria stenocephala* of dogs. Stiles, in 1902, demonstrated the fact that this parasite was not *Uncinaria stenocephala*, and he named it *Necator americanus*. Leiper has recently shown the wide distribution of this genus, and, like Ankylostoma, it is also the cause of ankylostomiasis in India. The parasite has been found on both continents, and is probably as widely distributed as Ankylostoma.

The chief points of difference between Necator and Ankylostoma are found in the buccal cavity in both sexes, and in the bursa copulatrix in the male; also in the size of the adults and of the eggs, which are slightly larger in Necator.

The Buccal Capsule.—Instead of hooks,



FIG. 195.—Necator americanus. *A*, male and *C*, female. (× 6 *after Placentia in Brumpt.*)



FIG. 196.—Anterior end of Necator americanus.

the buccal capsule is provided with two pairs of plates—one ventral, large, well developed, and easily seen, and one dorsal, relatively small, at each side of the dorsal and ventral median line respectively (Figs. 183 and 196). In addition to the single dorsal pharyngeal tooth (as in Ankylostoma) deep in the cavity of the buccal capsule, instead of one, Necator contains two pairs of submedial pharyngeal lancets or teeth—one dorsal and one ventral. The numbers of organs of attachment in Necator are, therefore, nine: four plates (two ventral and two dorsal); four submedial pharyngeal teeth or lancets (two dorsal and two ventral), and a dorsal conic tooth.

The Male.—The male is 7 to 9 mm. in length by 0.3 to 0.35μ in width. The bursa copulatrix is bilobed, instead of trilobed, as in Ankylostoma, this bilobed condition being due to a deep indentation of the dorsal rib toward the base, which almost divides it into two arms, each of which is bipartite instead of tripartite at the tip. There are, therefore, twelve ribs instead of eleven, the extra rib being formed by the division of the dorsal rib in two; apart from this the arrangement of the other ribs may be said to be somewhat similar in both genera. Two small precaudal papillæ can be seen anterior to the ventral ribs. The spicules are long (0.9 mm.) and slender and have a barbed point.

The Female.—The female measures 9 to 12.5 mm. in length. The vulva is situated in the anterior part, and near the middle of the body. The eggs measure, on an average, about 66 or 70μ by 40μ. They are,

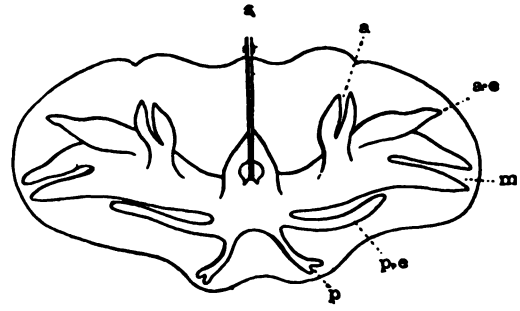


FIG. 197.—Necator americanus, bursa copulatrix. *S*, spicules; *a*, anterior ribs; *ae*, antero-external (lateral) rib; *m*, medial (lateral) ribs; postero-external (lateral) rib; *p*, posterior rib. (*After Stiles in Brumpt.*)

therefore, slightly longer than are the eggs of *A. duodenale*, but otherwise they may, for practical purposes, be said to be identical. The eggs of Necator, as passed with the feces, are said to be found in the eight-cell stage, whereas those of Ankylostoma are present in the four-cell stage, a point in the differentiation that is not reliable.

The *habitat, life history, mechanism of transmission, pathogenesis*, etc., of *Necator americanus* are the same as those of *Ankylostoma duodenale.*

4. **Œsophagostomum brumpti** (Brumpt, Railliet, et Henry, 1905).—This parasite is common in monkeys, especially in Africa, and is only occasionally present in man. Brumpt found the worm in cyst-like nodules in the cecum and colon of a negro in East Africa.

The body of the worm is white in color and cylindric in shape. There is a cuticular distention or collar in the anterior part of the body. The oral cavity is provided with twelve spines or papillæ and three sharp and slightly curved teeth. The male measures 6 to 8 mm. in length by 0.1 to 0.2 mm. in width. The *female* measures 8.5 to 10.2

mm. in length by 0.2 to 0.3 mm. in width. The vulva is situated at the posterior end, in front of the anus, which is subterminal.

The *life history* and *pathogenesis* are not known.

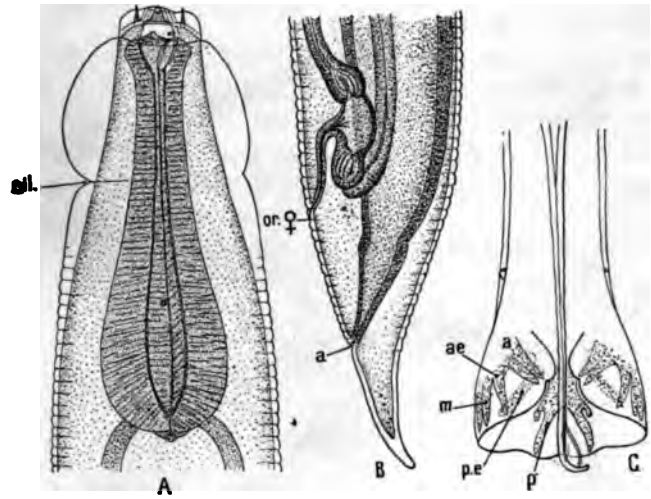


FIG. 198.—Œsophagostomum brumpti. *A*, cephalic extremity; *B*, caudal extremity of the female and *C*, bursa copulatrix of the male. *Sil*, ventral groove; *or*, genital pore; *a*, anus; *a*, *ae*, *m*, *ps* and *p*, ribs of the bursa; *sp*, spicule. (*After Railliet and Henry in Brumpt.*)

5. **Triodontophorus diminutus** (Railliet et Henry, 1905).—This parasite is common in monkeys, and in a few instances has been

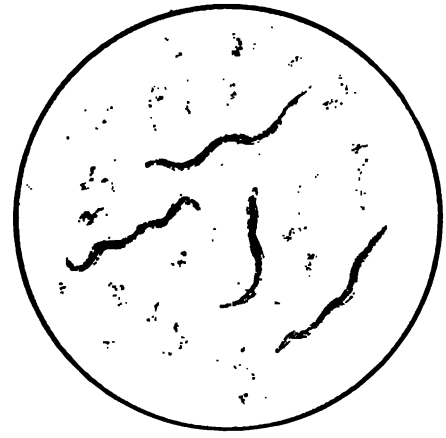


FIG. 199.—Larvæ of Esophagostomum brumpti in feces of monkey.

found in the large intestine of man. The male measures 9.5 mm. in length by 0.5 mm. in width. The female measures 11.7 mm. by 0.6 mm. The eggs are transparent, and 60μ by 40μ in dimensions.

The *life history* and *pathogenesis* are not known.

6. **Trichostrongylus instabilis** (Railliet, 1893).—This parasite is common in sheep and goats, and inhabits the duodenum of these animals, giving rise to a pernicious form of anemia. In a few instances it has been found in man.

The male measures 4 to 5 mm. in length. The bursa is bilobed, with two short spicules. The female is 4 to 6.5 mm. in length, the vulva being situated at the posterior fourth of the body. The eggs are elliptic, about 75μ by 45μ, and, as seen in the feces, are in the morula stage. The anterior part of the body is elongated in both sexes.

The *life history* and *pathogenesis* are unknown.

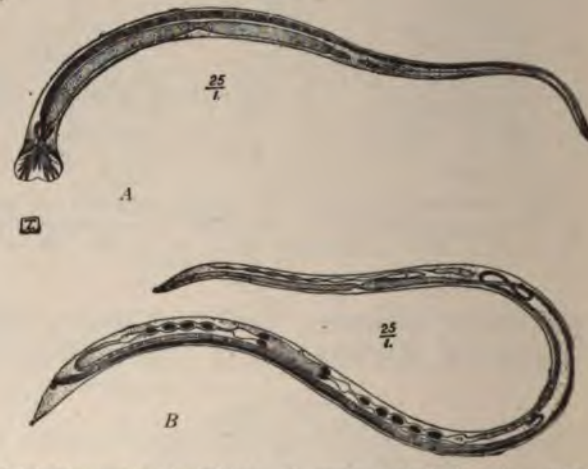


FIG. 200.—Trichostrongylus instabilis. *A*, male and *B*, female. (*After Manson in Brumpt.*)

7. **T. probolurus** (Railliet, 1896).—This worm is also a parasite of sheep, but was found by Looss in a man in Egypt.

The *life history* and *pathogenesis* are unknown.

8. **T. vitrinus** (Looss, 1905).—This parasite inhabits the duodenum of sheep. Looss found it in Egypt in 1905.

The *life history* and *pathogenesis* are unknown.

9. **Strongylus gibsoni** (Daniels, 1908).—This worm inhabits the stomach of hogs and cows, and is only occasionally found in man. The male is 21 mm. and the female 25 mm. in length. The long spicule, measuring 7 mm., is characteristic of the male.

10. **Physaloptera caucasica** (von Linstow, 1903).—This nematode has been found only once in the intestine of man. The male measures 15 mm. in length by 0.75 mm. in width; the female, 27 mm. in length

1 mm. in width. The eggs are thick shelled and measure 57μ by 39μ.

The *life history* is unknown.

11. **Physaloptera mordens** (Leiper, 1908).—This parasite resembles an immature *Ascaris lumbricoides*. It has been found in the



FIG. 201.—Strongyloides stercoralis (intestinalis) in the monkey (*Macacus cynomolgus*). *A*, female; *B*, male; *C*, male and female in copulation; *D*, embryo-egg; *E*, larva. (*A*, *B* and *C* × 150 *after Brumpt.*)

Transvaal in the stomach, esophagus, and small intestine of man. According to Leiper, the parasite may be differentiated from *P. caucasica* by the character of the caudal end of the male.

The *life history* and *pathogenesis* are not known.

FAMILY GNATHOSTOMIDÆ

Gnathostoma siamense (Levinsen, 1889).—This nematode is a parasite of the stomach of cats, dogs, hogs, and oxen, and has been found once as an erratic parasite in the subcutaneous tissue of man. The specimen seen in man was that of a female measuring 9 mm. in length by 1 mm. in width. The organism has two lips and a row of bristles, eight in number, around the head, and is provided with spines on the anterior part of the body. The posterior end had a three-lobed prominence, at the base of which the anus opens.

FAMILY ANGIOSTOMIDÆ (Genus, Strongyloides Grassi)

Strongyloides intestinalis (Bavay, 1876). *History.*—This nematode was first seen by Normand in 1876 in the feces of man. It was origin-

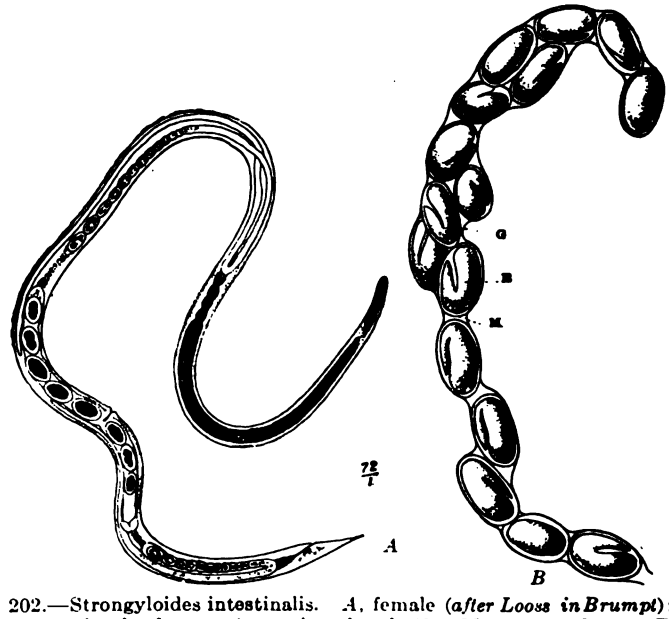


FIG. 202.—Strongyloides intestinalis. *A*, female (*after Looss in Brumpt*); *B*, chain of eggs as seen in the feces. *A*, uterine sheath (?); *M*, egg membrane; *E*, embryo. (× 200 *after Brumpt.*)

ally believed that there were two distinct species: One, *S. stercoralis*, a free living form found in the feces and in the soil; the other, *S. intestinalis*, the parasitic form found in the intestine of man. Leuckart showed that these were but succeeding generations of the life cycle of the same worm.

Only the female has been found in the small intestine of man. It is very small, measuring 2.2 mm. in length by 34μ in width. The mouth has four lips. The esophagus is cylindric and very long, ex-

tending for about one-fourth of the body length. The anus is in front of the tip of the tail. The eggs may be seen within the worm. They are few in number (8 to 12), elliptic in shape, and measure 50 to 58μ by 30 to 34μ. As found in the feces, the eggs are arranged in a chain surrounded by a common transparent sheath or glandular culdesac. They are greenish in color, and contain a completely formed embryo. They occur in the feces, especially during attacks of diarrhea.

Habitat.—The parasite is found in the duodenum and jejunum, embedded in the mucosa of the intestine.

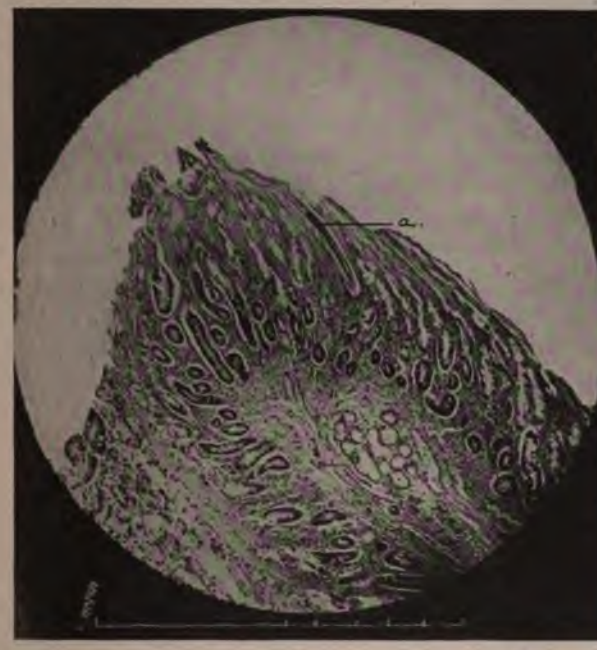


FIG. 203.—Adult Strongyloides intestinalis, *a*, in duodenal mucosa. (*Gage.*)

Life History.—Inasmuch as only the female has been found in man, it is believed that the worm is either hermaphroditic early in life, the male organs degenerating after fertilization, or that it is a parthenogenetic female. It is possible that, like Trichinella, both sexes exist during early development, but that the male lives only a very short time and dies after copulation.

The eggs, containing a completely formed embryo, are oviposited in the lumen of the intestine and discharged with the feces. These embryos hatch on the exterior and grow to adult male and female worms (*S. stercoralis*), which conjugate, the female laying eggs. These eggs, like those of Ankylostoma, give rise first to a rhabditiform and

then to a strongyloid or filiform larva. The Strongyloides larva, like Ankylostoma, may enter the host through either the skin or the mouth, and on reaching the intestine will burrow into the Lieberkühn follicles, grow to adult size, when the cycle is repeated.



FIG. 204.—Ova of Strongyloides intestinalis in crypts of duodenum.

Mechanism of Transmission.—The infective stage of the parasite is represented by the strongyloid larva seen in the soil, and infection takes place either by the larva penetrating the skin or through the mouth, through the medium of contaminated fingers, food, water, etc.

Pathogenesis.—This parasite has been regarded as non-pathogenic, but it is generally believed that in some instances it gives rise to a catarrhal condition of the small intestine (Cochin-China diarrhea).

Diagnosis.—As the parasitized person may not present any symptoms, the diagnosis is commonly dependent upon finding the eggs or the larva in the feces. When possible, the feces should be examined during an attack of diarrhea or after the administration of a purgative.

Treatment.—Medicinal treatment is usually without effect, as the parasite is hard to dislodge from the intestinal mucosa.

Prophylaxis.—The prophylactic measures are similar to those outlined for Ankylostoma.



FIG. 205.—Rhabditiform embryo of Strongyloides intestinalis as found in human feces. (*After Looss in Castellani and Chalmers.*)

FAMILY TRICHINELLIDÆ

1. **Trichuris (Trichocephalus) trichiuras** (Linnæus, 1771).—This nematode, commonly known as the "whipworm," from its characteristic resemblance to a whip, can be recognized without difficulty by its long and slender cephalic prolongation or neck, which constitutes over one-half of the whole length of the body, and which corresponds to the length of the esophagus. The *male* worm is from 30 to 45 mm. in length, and has a spirally coiled posterior end, provided with a spicule about 2.5 mm. in length, which lies in a retractile pouch. The *female* measures 45 to 50 mm. in length. The eggs are oval, brown, thick shelled, and provided with a clear knob at each pole. They measure about 50 to 54 by 23μ.

Habitat.—This parasite inhabits the cecum and appendix. In a few instances it has been found in the colon and small intestine.

Life History.—The eggs, as found in the feces, contain only one cell. Exteriorly the cell divides and gives rise to an embryo inside of

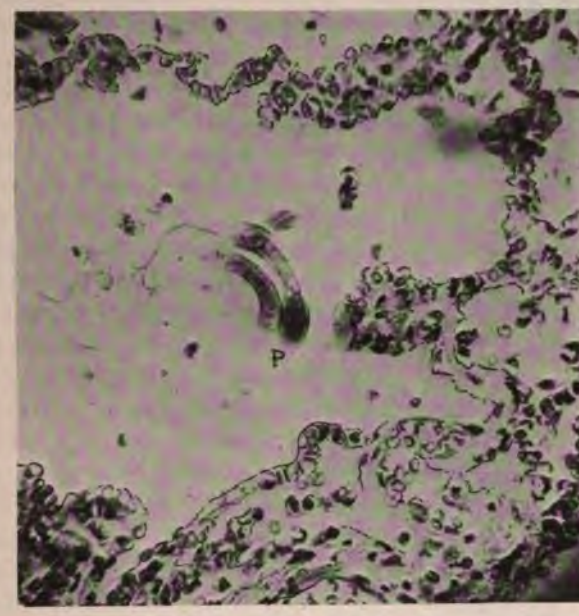


FIG. 206.—Larva of Strongyloides intestinalis in air sac of lung. Sections through two coils of the parasite, *p*, are shown. (*Gage.*)

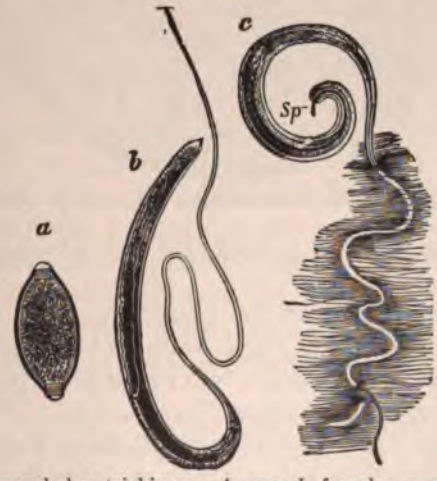


FIG. 207.—Trichocephalus trichiura. *A*, egg; *b*, female; *c*, male attached to the intestine showing the slender and long cephalic end buried in the submucosa; *sp*, spicule. (*After Leuckart in Brumpt.*)

the egg shell, which takes from six to twelve months to mature. This embryo, when carried into the mouth with contaminated water,

food, etc., is set free, passes to the intestine, attaches itself to the mucosa, and grows, reaching maturity in about four weeks. Development is, therefore, direct. As the egg, when discharged with the feces, contains only one cell and not a larva, direct auto-infection cannot occur, as is the case with Oxyuris.

Mechanism of Transmission.—Trichuris is transmitted through the mouth by means of contaminated food, water, etc. The infective stage of the parasite is represented by the embryo inclosed in the shell of the egg.

Pathogenesis.—This worm is one of the most common parasites of the intestine and is cosmopolitan in its distribution. Its presence in man, however, may not give rise to any appreciable symptoms. Under certain conditions, as in cases of marked infection, or when it is lodged in the appendix, it may give rise to appendicitis (Fig. 209) or predis-

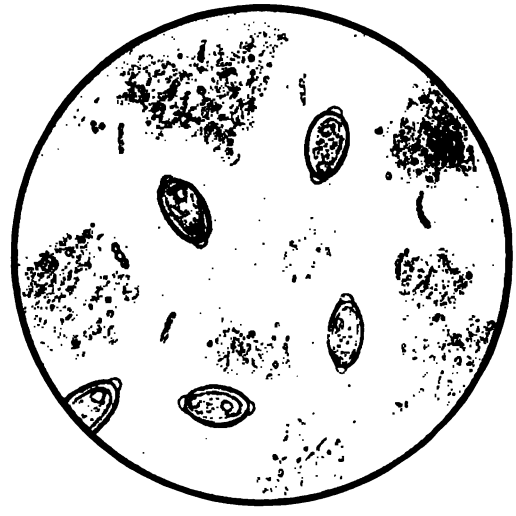


FIG. 208.—Ova of Trichocephalus trichiuris in the feces.

pose to the development of a variety of morbid changes in the body known as trichocephaliasis.

It was long believed that the parasite received its nourishment entirely from the contents of the intestine, but after the observations of Askanazy, Guiart, and others, who found blood pigment and also, in a few instances, fresh blood in the lumen of the intestine of the parasite, it is now conceded that this nematode also feeds on blood. The mode of fixation of the parasite is by means of the long and slender cephalic prolongation, which is thrust between the mucosa and into the muscularis of the intestine. This permits the infliction of injury on the capillaries and enables the worm to suck the extravasated blood.

The amount of blood taken may not be sufficient to produce any appreciable symptoms, *e.g.*, anemia, etc., but the injury to the mucosa may be the source of intestinal infection by bacteria, and this explains the common association of Trichiuris with typhoid fever, cholera, dysentery, appendicitis, and other intestinal derangements and constitutional disturbances, such as anemia, etc.

Diagnosis.—Since the presence of the parasite in man may not give rise to any typical symptoms, a positive diagnosis can be made only by finding the eggs in the feces. This, as a rule, offers no difficulty since they are commonly present and easily recognized. Sometimes the adult worm is found in the feces. The eosinophiles are usually increased in number.

Treatment.—So far as is known, the parasite is refractory to any form of medicinal treatment. This is explained by the mode of fixation of the parasite below the submucosa by means of the long cephalic prolongation, which serves as a very efficient means of attachment and also protects the worm against the deleterious action of drugs.

Prophylaxis.—The prophylaxis consists in thorough cleansing of the hands, avoidance of the use of impure water, disinfection of the feces, etc., and other indications as directed under Ascaris and Oxyuris.

When properly observed, these prophylactic measures constitute the only efficient treatment, for, by preventing a reinfection, the existing worms will in time die and disappear. The life duration of the worm is not known, but, judging from other parasites, it probably does not live longer than from two to five years. It is possible, therefore, that if reinfection is prevented, a parasitized person may be free from the parasite in that time.

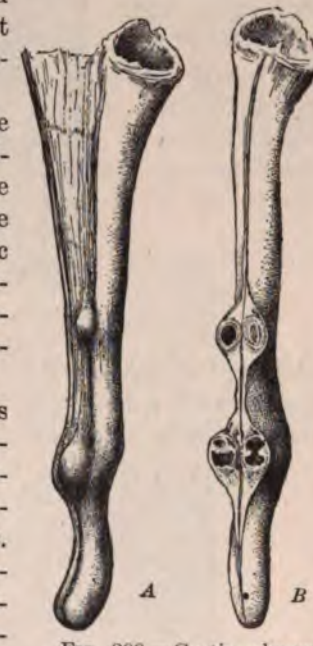


FIG. 209.—Cystic changes of the appendix due to trichocephalus. *A*, before and *B*, after section of the cyst. (*After Brumpt.*)

2. Trichinella spiralis (Owen, 1835). *History.*—The presence of minute cysts in the voluntary muscles of man was observed by Peacock in 1828, by Hilton in 1832, and by Paget at about the same time, but the nature of the cyst was established by Owen in 1853. The researches of Leuckart in 1855, of Virchow in 1859, and of Zenker in 1860 confirmed the main principles regarding the parasitic nature of this affection.

With the exception of *Strongyloides intestinalis*, this parasite is the smallest of all the parasitic nematodes of the intestine. It is very slender, and barely visible to the naked eye. It is whitish in



FIG. 210.—Trichocephalus suis. Attached to mucosa of cecum of hog.

color, and characterized by the presence of a tapering and elongated anterior end, a long cylindric esophagus, and a thick posterior end, which gives the worm a club-shaped appearance.

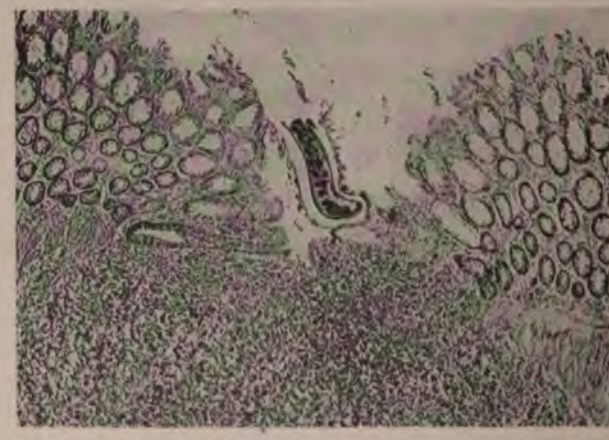


FIG. 211.—Trichocephalus trichiura close to intestinal attachment. The subjacent round cells are those of a solitary lymphoid follicle.

The *male* measures 1.4 to 1.6 mm. in length by about 40μ in width in its largest diameter. The posterior extremity is provided with a pair of well-developed papillæ, at the base of which the cloacal orifice

is situated. Posterior to the cloaca two pairs of papillæ or plates are seen.

The *female* measures 3 to 4 mm. in length by about 60μ in width. The vulva is situated at about the anterior fifth of the body; the anus is terminal. The worm is viviparous; that is, it gives birth to a completely formed free embryo, which, when discharged in the lumen of the intestine, reaches the blood-stream and becomes lodged in the muscle, where it undergoes encystment.

The *cysts* appear as minute white specks, oval in shape, their long axes running in the direction of the muscle-fibers. They measure about 400μ by 250μ, and under magnification are seen to contain a coiled-up larval embryo. In severe infestations more than one embryo may be seen inside of the cyst. The cyst is surrounded by a membrane formed from the surrounding tissue. In this resting stage the worm may live for years. The cysts are found chiefly in the diaphragm, the muscles of the larynx, tongue, and abdomen, and in the intercostal muscles and near the tendons. They may be found in any of the voluntary muscles, and may be so few in number as to escape detection or may number millions.



FIG. 212.

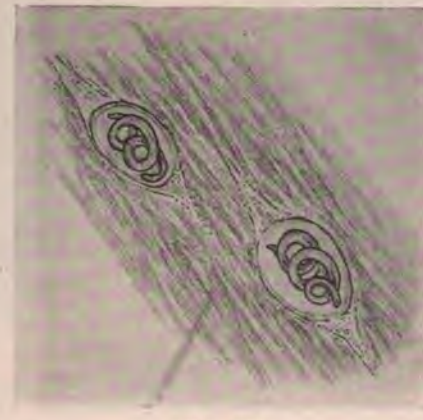


FIG. 213.

FIG. 212.—Adult Trichinella spiralis. ♀, male and ♂, female. *E*, esophagus; *Int*, intestine; *An*, anus; *Cl*, cloaca; *T*, testes; *Vd*, vas deferens; *Gp*, genital pore; *Va*, vagina; *Ut*, uterus; *Ovd*, oviduct; *Ov*, ovary.

FIG. 213.—Mounted preparation of the diaphragm of a white rat showing trichinella embryos encysted between the muscle fibres.

Habitat.—The Trichinella is in reality a parasite of the black rat (*Mus rattus*) and the gray rat (*Mus norvegicus*), in which animals the infection is placed at from 8.3 to 100 per cent., according to the

locality. It may, however, spread from rats to dogs, cats, hogs, and many other mammals. The hog is infested from infected rats, and man becomes infested from the hog by eating improperly cooked pork containing the encysted larvæ. In experimental cases the adult parasite is seen to inhabit the small intestines, or, when the infection is very marked, it may also be found in the large intestine. The encysted larvæ, as previously stated, inhabit the voluntary muscles. Under normal conditions birds and cold-blooded animals are refractory to the parasite.

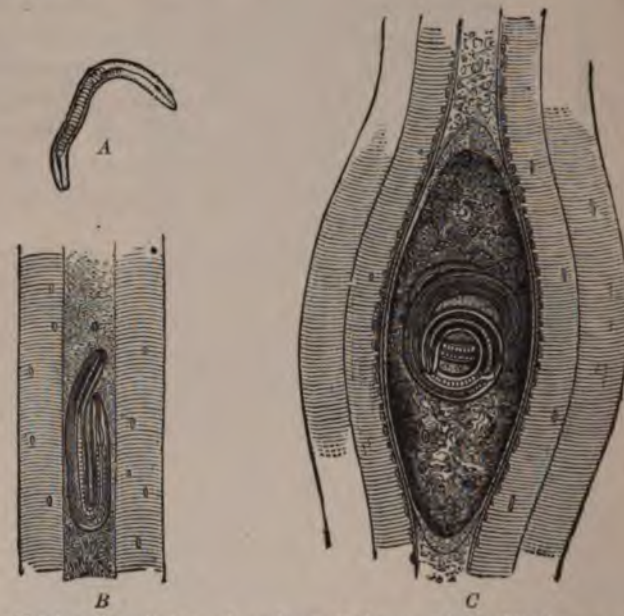


FIG. 214.—Trichinella spiralis. *A*, embryo; *b*, the same lodged in the muscle before encystment; *c*, encysted larva, 15 days old. (*After Claus in Brumpt.*)

Life History.—The life history of *Trichinella spiralis* can easily be followed experimentally, since it is only necessary to feed a series of rats with trichinized meat and sacrifice them at intervals. The cyst is digested in the stomach of the rat, the embryos escape, and in from two to four hours after they can be found free in the stomach and in the lumen of the duodenum. In the duodenum and in the upper part of the jejunum, after twenty-four hours, the embryos begin to grow very rapidly, and in from forty-eight hours to three or four days they become sexually mature (Fig. 222). Fertilization takes place on the third day, and the development of the egg in the uterus of the female can easily be followed. The eggs in the uterus, when matured, measure about 20μ in diameter, and contain well-developed embryos, which hatch, and falling into the uterus, make their way to-

ward the anterior part of the body. On the sixth or seventh day after infestation they begin to be discharged by the females, but before this happens the female migrates toward the wall of the intestine and bores her head like an ovipositor, into a lacteal vessel or into the mucosa and submucosa (Fig. 216) and discharges the embryos directly into the lymphatic capillaries.

The embryos now migrate passively or by their own activity into the lymphatic vessels, and are carried by the thoracic duct to the heart, where they are disseminated with the blood-stream over the entire body. On reaching the capillaries they leave the circulation and become lodged between the fibers of the voluntary muscles, where they undergo encystment and development.



FIG. 215.—Trichinella larva escaping from the cyst, digested in vitro by artificial gastric juice.

The embryos may also pierce the wall of the intestine and fall into the peritoneal cavity, where they may be found in great numbers between the second and fourth weeks after infestation. Migration of the embryos by way of the portal system is possible, but has not been demonstrated.

The embryos (Figs. 217 and 218), as found in the peritoneum, in the thoracic duct, or in the blood of the heart and large blood-vessels, are slightly thickened posteriorly, provided with a mouth and a rudimentary intestinal tract, and measure from 90 to 100μ in length by about 6μ in width.

Encystment.—The point of encystment of the embryo is still a disputed question. According to some authors (Virchow, Leuckart, Hertwig, etc.), the embryos on leaving the capillaries, enter the muscle-fibers and encystment takes place within the sarcolemma sheath (Fig. 219). Other authors (Chatin, Delavaux), however, assert that encystment takes place in the connective tissue between the muscle-fibers, as in the case of cysticercus. Whichever statement is correct, the fact remains that the cyst, as usually seen, appears between the muscle-fibers, which gradually separate and undergo pressure atrophy and degeneration as the cyst increases in size.

The presence of the embryo in the muscle is the source of irritation, which first gives rise to a hyperplasia and then to pressure atrophy and degeneration of the surrounding fibers. The embryo is also the cause of a mild degree of chronic inflammation, which in time gives rise to the formation of a delicate fibrous capsule derived from the tissues of the host around it.

The time required for the complete formation of the cyst is about fifteen days, and corresponds to the growth of the embryo from the time it lodges in the muscle until it has reached the encapsulated or resting stage. During this time the embryo increases in size from 90 to 100μ up to about 900μ or 1 mm. in length by 6 to 8μ in width.

When fully formed, the cyst is oval in shape and about 400μ in length by about 250μ in diameter. It usually contains a single embryo coiled spirally or arranged in a figure-of-eight shape. In cases of marked infestation as many as two or three or even seven embryos (Orren, Chatin) may be found in a single cyst. On being swallowed

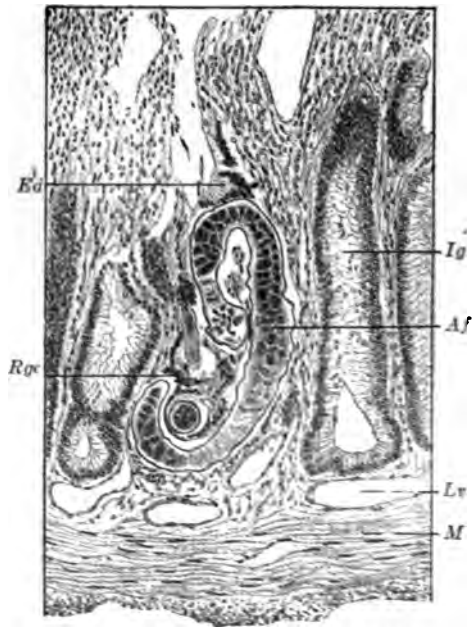


FIG. 216.—Trichinella spiralis. Section of the intestine of a rat 10 days after infestment. *Ed*, epithelial detritus; *Ig*, intestinal gland; *Af*, adult female; *Rgc*, remnant of glandular cul de sac; *Lv*, lymph vessel; *M*, muscular layer. (*After Braun.*)

by another host these cysts are set free in the stomach, pass to the intestine, grow to maturity, and the cycle is repeated.

The time occupied in completing a cycle in the life history of *Trichinella spiralis* is from twenty-three to twenty-five days. This period may be divided up as follows:

(1) From the fertilization of the egg in the uterus to the discharge of the embryo—five days; (2) from the discharge of the embryo in the intestine of the host to complete encystment in the muscle—about fifteen days; (3) from complete encystment in the muscle to maturation and fertilization of the female in the intestine—three to five days.

It may be recalled, as stated elsewhere, that although the life history of the parasite requires two hosts for its completion, the second host is essential only for transmitting the worm to another animal, and not because, in the absence of this secondary host, the life cycle will not be completed, as is the case with the malarial parasite, most cestodes, etc. Strictly speaking, in a biologic sense, *Trichinella spiralis* requires only one host to complete its life history. This is proved by the fact that, as previously explained, if an infested rat is fed experimentally with its own flesh, containing the encysted embryos, the embryos will grow to maturity and give birth to new embryos in the intestine and to new cysts in the muscle of the same animal (Rivas).



FIG. 217.



FIG. 218.

FIG. 217.—Trichinella embryos in the peritoneal exudate of a white rat ten days after infection.

FIG. 218.—Trichinella embryos in the blood from the heart of a white rat ten days after infestation. Preparation made by the acetic acid concentration method.

Vitality of the Encysted Embryos.—In the encysted or resting stage the embryo may remain alive for a very long time. Thus in man it may live five years (Grienpenkerl), twelve years, (Tungel), or even longer—twenty-five years (?). As a rule, however, its life is much shorter, for the cysts become calcified in the course of several months or a few years.

When lodged in the muscles, the cysts may resist putrefaction for three months. In fresh ham they withstand a temperature of − 22° to − 25° C. for three days (Leuckart). Isolated cysts placed between two slides are destroyed at a temperature of 48° to 50° C. in ten minutes, but when massed in meat about thirty minutes boiling per kilogram of weight is necessary for their destruction. Salting, souring, and smoking exert their effect only on the cysts in the outer portion of the meat.

Artificial Cultures.—Trichinella embryos can easily be studied by employing artificial gastric juice which is made as follows: To pepsin, 0.5 gr., and hydrochloric acid, 0.2 to 0.5 c.c., add water, 100 c.c. The meat containing the Trichinella cysts is finely chopped and a small portion placed in a test-tube; to this about 5 c.c. of the artificial gastric juice is added. The tubes are incubated at 37° C. for several hours, or kept at room temperature over night. When the cyst is digested the embryos escape and may be seen under the microscope in preparations made from the bottom of the tube (Fig. 221).

The free larvæ may remain alive in this medium for two or three days, but if the gastric juice is removed by centrifugalization and decantation and replaced by a neutral or slightly alkaline medium,



FIG. 219.



FIG. 220.

FIG. 219.—Trichinella larva entering muscle fiber. An acute myositis is associated, shown by nearby cellular infiltrate and proliferation of muscle fiber nuclei.

FIG. 220.—Old cysts of trichinella.

such as 1 per cent. gelatin, bouillion, or physiologic salt solution, they may live longer. By this method the larvæ may be kept alive for about one week.

The writer conducted a series of experiments with artificial cultures for the purpose of determining the growth of the larvæ *in vitro*, but obtained negative results. After several days a few of the larvæ were seen to measure from 1000μ to 1200μ in length, but no further development of the digestive tract, beyond that seen in the common encysted forms, was observed, nor was there any indication of development of the sexual organs. Frequently a few larvæ measuring 1300μ or a little more were seen in the culture, but these were not alive, and

the apparent increase in size was due perhaps to a natural relaxation of the larvæ after death.

Mechanism of Transmission.—The infective stage in the life history of *Trichinella spiralis* is represented by the encysted larvæ as found in the muscle. Man becomes infected only through the mouth, by eating improperly cooked meats containing the cysts. The most common source of infection is pork, especially sausage.

Pathogenesis.—The presence of Trichinella in man gives rise to a group of morbid changes in the organism known collectively as trichiniasis. The adult parasite exercises its pathogenic action on the small intestine, whereas the embryos attack the muscle. The symptoms

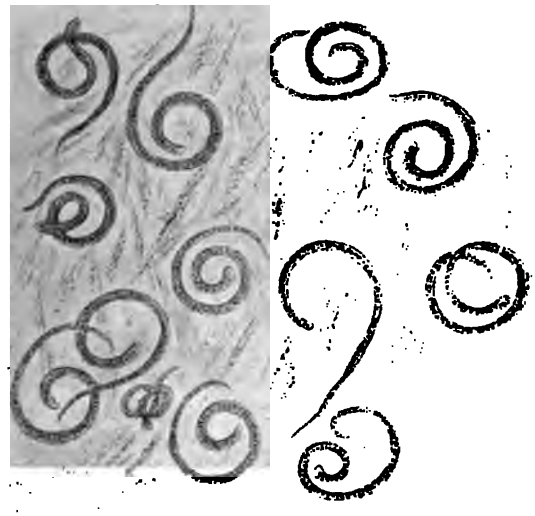


FIG. 221.—Young free larvæ of Trichinella spiralis as seen in vitro from a two days old culture in artificial gastric juice.

common to the affection are, therefore, those of a general catarrhal enteritis, more or less intense, accompanied by generalized or constitutional disturbances. The course of the disease may properly be divided into four periods, which correspond to the various stages of development.

First Period.—This corresponds to the first phase of the infection, when the embryos are being set free in the stomach and pass to the small intestine. The ingestion of a large quantity of parasitized meat may give rise to a catarrhal inflammation of the whole intestinal tract that is so intense in some cases that it may cause death from in twenty-four to forty-eight hours. These violent symptoms are rare in man, but are commonly seen to occur in animals used for laboratory experi-

ments in which there is a tendency to give excessive doses of the parasitized material. These acute symptoms are due to mechanical and perhaps also to toxic irritation produced by the parasites in the lumen of the intestine, which not uncommonly may give rise to extensive hemorrhages. Choleric or dysenteric diarrhea, nausea, vomiting, and pain may occur, and the temperature may rise to 102° or 104° F. or higher. This first stage lasts about one week.

Second Period.—Toward the end of the first week the embryos begin to traverse the wall of the intestine and become lodged in the muscle. Fever, general debility, delirium, rheumatic and general muscular pains, labored respiration, and painful mastication and deglutition may occur. This second period lasts about one or two weeks.

Third Period.—This corresponds to the period of encystment. Toward the middle of the second or third week after infection the embryos begin to lodge in the muscles. Edema of the face, cachexia, general mental and physical debility, pruritus, and skin eruptions may occur. This stage lasts for about one week.

Fourth Period.—In mild cases the acute stage lasts only two or three weeks, but in cases of severe infection it may last from six weeks to three or four months. When death occurs it usually takes place between the second and seventh week, usually on the third week and is generally due to cachexia, pulmonary or cutaneous complications, severe gastro-intestinal derangement, toxemia, or bacterial infection. When the case terminates favorably, the temperature returns to normal, the edema disappears, and all the other symptoms subside. Muscular pains, more or less intense and not uncommonly periodic and irregular in character, resembling attacks of rheumatism, and occasionally cramp, may continue for several months or years.

Clinical Diagnosis.—In very mild cases the symptoms may be so atypical that the disease may easily be mistaken for a simple attack of indigestion. In more severe cases the sudden onset of the gastro-intestinal symptoms may simulate intestinal intoxication, and if accompanied by continued fever, may resemble typhoid fever. Finally, when edema appears, trichiniasis may be mistaken for nephritis, and in the chronic stage for rheumatism. Since, therefore, trichiniasis is not attended by any typical symptoms, the diagnosis is not uncommonly made by exclusion.

In *acute indigestion* the symptoms are apt to be very mild and of short duration, disappearing after from twenty-four to forty-eight hours either without treatment or after the administration of a purgative.

In *intestinal intoxication* the gastro-intestinal symptoms are more severe, but they not uncommonly disappear in two or three days under appropriate treatment, such as emetics, purgatives, proper diet, and the administration of intestinal antiseptics.

The Widal reaction will readily differentiate *typhoid fever* from trichiniasis; moreover, eosinophilia is present in the latter condition.

When edema is present, the absence of albumin in the urine in trichiniasis is a valuable point in differentiating it from *nephritis*.

The chronic stage of trichiniasis may resemble *rheumatism* so closely that the diagnosis can be made with certainty only by the presence of eosinophilia and the finding of the cysts in the muscles. This may be accomplished by examining a small piece of muscle removed from the leg, as near the tendon as possible, under the miroscope.

During the first week of the disease the epidemiology of trichiniasis may furnish a most important point in the diagnosis, thus trichiniasis is apt to be a house disease; that is, two or more members of a family



FIG. 222.—Adult Trichinella spiralis ♂, and ♀, female from the duodenal contents of a white rat, ten days after infection, as seen under the low power of the microscope.

who have eaten the infested meat during the day will display the same symptoms at about the same time. *Mushroom poisoning* is apt to show similar epidemiologic features, but in this form of poisoning the toxic symptoms predominate and the disease is of short duration terminating either in recovery or in death within a few days.

Laboratory Diagnosis.—Examination of the blood during the first few days of the disease (forty-eight to seventy-two hours (Rivas) or near the end of the first week shows an increase of eosinophiles above the normal (1 to 3 per cent.). About this time, and more especially during the second week, the adult parasite, male and female, and the embryos may be found in the feces. This is not, however, an easy task, since the minute size of the parasite makes its detection difficult. Repeated examination under the microscope, or by the aid of a magni-

fying lens, of a fresh cover-glass preparation made from the feces during the diarrheal attack, if possible, or after the administration of thymol and saline purgative, may show the presence of the parasites.

In the second or third week of the disease the embryos undergo encystment, and at this time and subsequently the trichinella cysts may be found in the muscle. The method of procedure is as follows: A small incision is made on the outer side of the leg and a piece of flesh removed as near the tendon as possible. This material is placed on a slide with a few drops of a 5 per cent. acetic acid solution, teased with a pair of dissecting forceps, covered with another slide, and examined under the lower power of the microscope or with a magnifying lens. When present, the trichinella cysts are easily recognized.

Treatment.—Medicinal treatment is always more or less effective. During the first weeks of the disease immediately after infestment, such as emetics, washing of the stomach and purgatives is recommended. The adult worms and the free embryos may be expelled by the anus after the administration of vermifuges, especially thymol, followed by a purgative. Nothing can be done to detach the encysted embryos, and the subsequent treatment is merely symptomatic.

Prophylaxis.—The prophylactic measures to be employed in trichiniasis may be summarized as follows:

1. Restriction of the infestation of pigs by the destruction of rats in the pig pens, stables, and surrounding places. These animals should not be fed with the refuse of meat improperly cooked.

2. Inspection of meat in the abattoirs. The well-organized system of meat inspection carried out in Germany, where a veritable army of inspectors is in charge of the control, has greatly reduced the number of cases of trichiniasis in that country. The method employed is as follows: A small fragment of the diaphragm is removed, placed between two slides in a 1 to 5 per cent. solution of acetic acid, and examined with a magnifying lens. In cases of mild infestation the meat is finely chopped, digested in artificial gastric juice, and the sediment examined.

3. The use of improperly cooked pork, especially sausage, should be avoided.

II. NEMATODES OF THE LYMPHATICS AND BLOOD

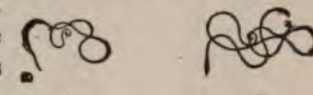
FAMILY FILARIDÆ

1. **Filaria bancrofti** (Cobbold, 1877). *History.*—The microfilaria of the parasite was first discovered in Paris by Demarquay, in 1863, in the chylocele fluid of a patient. Wucherer, in 1866, found it in the urine in a case of chyluria, and his findings were corroborated by Salisbury, Lewis, and Cobbold. In 1872 Lewis found the embryo in the blood

and named the parasite *Filaria sanguinis hominis*. Bancroft, in 1876, discovered the adult female, and Borne, in 1888, found the adult male.

Since 1875, as the result of numerous observations upon the parasite, Manson regarded it as the cause of elephantiasis and a certain number of diseases of the lymphatic system (lymph scrotum, adenolymphocele, etc.), and in 1878 the same author suggested the possibility that the parasite was transmitted by the mosquito. Manson believed that the microfilaria escaped from the insect into the water, and thus infected man; later, however, in conjunction with Bancroft, he concluded that the parasite was directly transmitted by the bite of the mosquito.

The researches of Bancroft, Low, James, Fülleborn, Lebredo, and others have demonstrated that microfilariæ, taken into the body of a mosquito with the blood of an infested human being, migrate to the muscles of the thorax of the mosquito, and there undergo development and grow into larvæ. They then pass to the mouth of the insect, and are subsequently transmitted to other persons when bitten by the mosquito.



A *B*

FIG. 223.—Filaria bancrofti. *A*, male and *B*, female. Natural size. (*After Manson in Brumpt.*)

Similar observations have been made by Grassi and Noè on the filaria of the dog (*F. immitis*), except that, in this case the microfilaria undergoes development in the Malpighian tubules instead of in the thoracic muscles of the insect.

Description.—The adult filarial worm is filiform in shape and whitish in color. The cuticle is smooth. The head is globular, and the mouth is terminal, circular, unarmed, and devoid of lips.

The *male* is smaller than the female, and is easily recognized by its corkscrew-like curve at the tail. It measures about 40 mm. in length by about 0.1 mm. in width. The anus is situated about 130μ from the posterior end and between two projecting papillæ. The anal papillæ are not well defined; according to Looss, there are three pairs of preanal papillæ. The spicules are unequal, two in number, and measure 0.6 and 0.2 mm. respectively.

The *female* worm measures 80 to 100 mm. in length by 200 to 300μ in width. The vulva is situated anteriorly, about 1 to 1.3 mm. from the mouth, from which two uterine tubes run internally along the greater length of the body. The tubes contain the eggs and embryos in various stages of development.

Habitat.—The adult inhabits the lymphatic ganglia of the pelvis and abdomen. The parasites are also found in cystic dilatations in the subcutaneous tissue, the scrotum, lymphatic varices of the arms, legs, etc. The microfilariæ which are discharged in these localities

are carried by the lymphatics into the blood-stream by way of the thoracic duct, and are found, especially at night, in the peripheral blood. The male and female filariæ are present together, the males being fewer in number than the females. If placed in saline solution while alive, the parasites display active movements for hours.

Habitat and Morphology of the Embryo.—As has been previously stated, the eggs may be seen in all stages of development in the uterus. The egg proper, as seen at the beginning of the uterine tube, is slightly oval, about 50 by 34μ in size, and undergoes cleavage and development, becomes larger and elongated, until, in the anterior part of the uterus, it is seen to contain a fully formed embryo. The embryo, or microfilaria, finally escapes through the genital pore, which is situated in the anterior part of the body, about 1 mm. from the mouth, and,

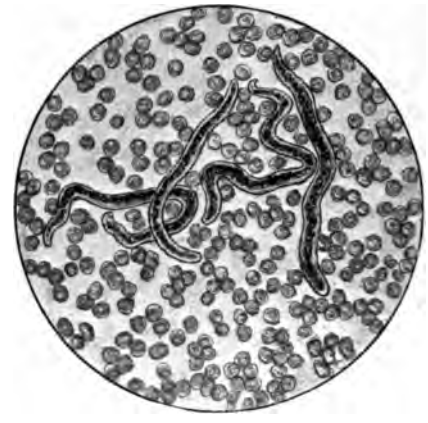


FIG. 224.—Microfilaria bancrofti in human blood.

entering the lymph-stream, lymphatic vessels, and thoracic duct, it finally reaches the heart and the blood-stream. The microfilariæ, as stated, are more abundant in the peripheral circulation at night.

Fresh cover-glass preparations, seen under the low power of the microscope, show the microfilaria (Fig. 224) to be small, wriggling, filiform bodies, tossing the blood-cells about, actively motile, but not moving away from the field of the microscope. They are from 130 to 300μ in length by 7 to 11μ in width. It may be noted that the microfilaria is slightly wider than the diameter of the red blood-cells, and about twice as large as the lumen of the capillaries, a fact that, as will be shown further on, explains the periodicity due to their retention in the peripheral blood.

Under a higher magnification the microfilaria is seen to be long, slender, and cylindric in shape, with a round anterior and a tapering posterior end. It is inclosed in a sheath—the vitelline or egg mem-

brane—which is much longer than the embryo, and inside of which it may be seen darting backward and forward.

The anterior rounded extremity is provided with a hemispheric proboscis containing a minute apical spine that is capable of being covered by a retractile and protractile six-lipped prepuce. The function of the spine is to pierce the sheath so that the embryo may escape. Normally, this takes place in the stomach of the mosquito, but it can also be observed in fresh cover-glass preparations that have been allowed to stand for some time.

The body of the microfilaria is transversely striated, and presents a granular appearance. This granulation is made up of embryonic cells so arranged as to leave certain clear spaces or embryonic spots, which are clearly seen in stained preparations. In the work of Manson, van Campenhout, d'Annet, Dutton and Elliot, six of these spots are described, which correspond to the embryonic structure for the future development of the adult worm: (1) A clear cephalic spot for the formation of the anterior part of the intestinal tract; (2) an anterior oblique spot, which is the "anlage" for the nervous system; (3) the anterior V spot of Manson, for the development of the excretory system; (4) the central part, for the development of the middle portion of the digestive tract; (5) the oval or tail spot of Manson, provided with a pore, which is the "anlage" for the anus in the female and for the cloaca in the male; (6) a small central spot at the caudal end, which is not always present, and which probably serves for the formation of the reproductive organs.

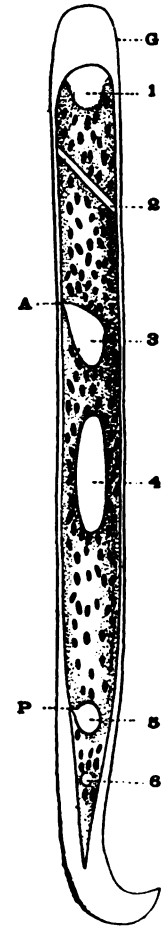


FIG. 225.—Diagram of a microfilaria. *G*, sheaths; 1, 2, 3, 4, and 5, anterior (cephalic) oblique, V-shape, central and posterior (caudal) spots respectively; 6, small terminal spot occasionally present. *A* and *B*, aulayre for the mater vascular system and hind gut respectively (*Manson*). *P*, proctodeum. (*After Brumpt.*)

The development of the worm, however, has recently been studied by Fülleborn. This author recognizes the presence of certain cells and structures in the microfilariæ which are the anlage for the future organs of the worm (Fig. 226).

Periodicity.—The microfilariæ of *F. bancrofti* are peculiar in that they are easily found in the peripheral blood at night and are apparently absent during the day. They first appear in the peripheral blood some time between 5 and 8 P. M., and steadily increase in number until midnight or until 4 A. M., when they gradually disappear. At about 7 or 9

A. M. only a few are found, and from 10 A. M. until 6 or 8 P. M. they are usually absent. They reappear after 8 P. M., and the cycle is then repeated. It will be seen, therefore, that a definite periodicity exists, but this is not absolute, as is generally believed, for, as a matter of fact, the embryos are constantly present in the peripheral circulation at all hours of the day and night, although a larger quantity of blood must be examined for their detection during the day, as is shown in Table I.

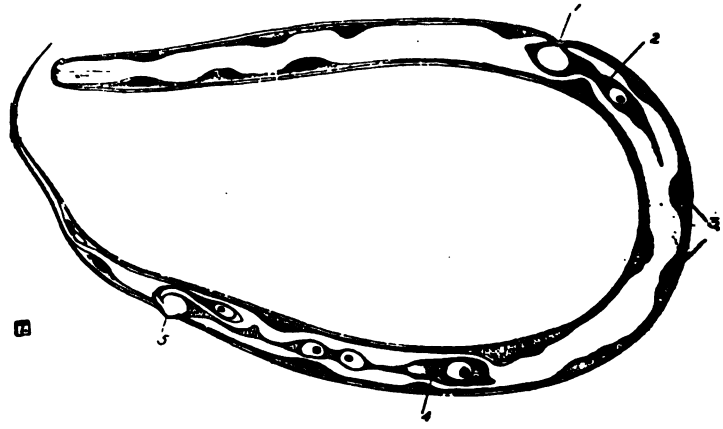


FIG. 226.—Scheme of the structure of a microfilaria, showing (1) the excretory pore; (2) the cells, which will form the excretory apparatus; (3) the subcuticular cells; (4) the genital cells; (5) the genital pore. (*After Fülleborn in Castellani and Chalmers.*)

TABLE I.—FILARIA NOCTURNA; PERIPHERAL BLOOD; TWENTY-FOUR-HOUR CYCLE

Hour of Examination	Fresh Cover-glass Preparation	
	In one slide, embryos	In several slides (about 0.05 c.c. of the blood examined), embryos
12 noon	0	4
2 P. M.	0	3
4 P. M.	0	2
6 P. M.	0	5
8 P. M.	0	8
10 P. M.	2	50
12 Midnight	15	75
2 A. M.	25	550
4 A. M.	30	300
6 A. M.	20	250
8 A. M.	10	80
10 A. M.	2	20

Various theories have been advanced to account for this periodicity; among these may be mentioned: (1) The theory of von Linstow, who

believed that the relaxation of the capillaries at night permits the embryos to enter the peripheral circulation; (2) the theory of Carter, who believed that an increase in the flow of chyle at night carried the embryos from the lymphatics of the pelvis and abdomen into the thoracic duct, heart, and blood-stream; (3) the theory of Myers, who suggested that a new crop of embryos is born every night and dies during the day. This theory deserves only a passing mention. As a matter of fact, the embryos live *in vitro* for more than one week, and probably for a month in the circulating blood (see Table IV). (4) The adaptation view, which holds that the embryos come to the peripheral circulation at night, so that they may enter the mosquito to complete their life cycle; (5) the chemotactic or chemotropic theory of Manson, who believed that some substance was present in the capillaries at night that attracted the embryos—a theory that does not clear up the problem; (6) variations in atmospheric temperature, light, or darkness seem to have no effect, and the pulse-rate alone is not responsible; (7) Mackenzie and Manson have long shown that this phenomenon is in some way connected with sleep, for the periodicity is reversed if the patient sleeps during the day instead of at night—an explanation which is also far from satisfactory.

In conjunction with Dr. Allen J. Smith the author has formulated a theory, based on observation and experimental data, that may serve to elucidate the periodicity with which the embryos appear in the peripheral blood. To this the name "Retention Theory" has tentatively been applied, and its description follows:

The Retention Theory.—Taking into consideration the fact that the microfilariæ, although actively motile, have no movement of progression of their own, since they are inclosed in a sheath; also that their diameter is from 7 to 9μ—that is, about one-third larger than an erythrocyte and about twice as large as the diameter of the capillaries; it is logical to assume, therefore, that the microfilariæ are carried passively by the blood-stream; that they display a tendency to be retained in the capillaries in general, as well as in the peripheral circulation, where these vessels are abundant; that for the passage of the microfilariæ from the arterial to the venous system, through these capillaries, the pumping action of the heart, nervous irritability, muscular activity, and external influences, such as pressure, etc., are required; that such conditions as sleep, weak heart, the lowering of external stimuli, etc., will further the retention of the embryos in these capillaries, whereas the opposite conditions will have a contrary effect.

These facts just cited may explain the cause of the periodic appearance of microfilariæ in the peripheral blood. Thus at night, when conditions favor the retention of the embryos in the capillaries, they are more abundant in these vessels, whereas during the day the

increased action of the heart, the nervous and muscular activity which is naturally more marked during these hours, and the external agencies, such as pressure, touch, and movement of the limbs and fingers, etc., all tend to facilitate the passage of the embryos to the venous system, with the result that they are more or less equally distributed in the bulk of the blood, and their retention in the capillaries being consequently less marked, the embryos are less abundant in the peripheral blood.

The question may be asked why the embryos are not found in the peripheral blood during the day. This, of course, is easily answered: as has previously been stated, the microfilariæ are more or less equally distributed throughout the blood, and, besides, the amount of blood examined should be taken into consideration. If, for example, in examining the blood in fresh cover-glass preparations, as is usually recommended, only about 1 to 2 c.mm. of the blood collected from the finger is employed, and that in the early stages of the disease or in a mild infestation only 1,000,000 embryos are circulating in the 5000 c.c. of blood in the body, there will be 200 embryos in 1 c.c. of blood, or 0.2 per c.mm. If the blood contains 5,000,000 embryos, as we observed in one of our cases, there will be about 1000 embryos per cubic centimeter, or 1 per c.mm., which can easily be overlooked in the preparation, and which would explain the negative finding, whereas in marked infestation, in which 10,000,000 or even 30,000,000 embryos have been estimated as being present in the blood, as reported by Manson and others, the microfilariæ would be found without difficulty during the day. The periodicity of microfilariæ is, therefore, merely relative, since they are always found during the day and night in the peripheral blood if sufficient blood is examined, as is shown in Table III.

We believe, therefore, that the "Retention Theory" offers a very simple, clear, and plausible explanation for the periodicity of the microfilariæ of *Filaria bancrofti* in the peripheral circulation. Moreover, since other microfilariæ which are naked, that is, without a sheath, can consequently traverse the capillaries as the result of their own activity, and in those in which the sheath is closely applied to the cuticle, as well as those whose diameter is less than that of a red blood-cell, the periodicity is either absent or inappreciable. This is well illustrated by the microfilariæ of *F. perstans*, in which the absence of a sheath and the small diameter of the embryo permit it to gain easy access through the capillaries, the parasite acting very much like a trypanosome in the blood. That the periodicity of all microfilariæ bears a direct relation to the structure and size of the embryos and the resistance that the capillaries offer to their passage,

the capillaries acting, therefore, as a filter, is clearly illustrated in Table II.

TABLE II.—COMPARATIVE PERIODICITY OF VARIOUS MICROFILARIÆ IN THE PERIPHERAL BLOOD

Name	Host	Habitat of Adult	Average Size of Embryo in Microns	Presence of Sheath	Periodicity
F. bancrofti.....	Man	Lymphatics of abdomen and pelvis	220 by 9	yes	Nocturnal
F. taniguchii.....	Man	Lymphatics of groin	160 by 8	yes	Nocturnal
F. loa.....	Man	Subcutaneous tissue	220 by 9	yes	Diurnal
F. perstans	Man	Mesentery	100 by 4	no	Absent
F. ozzardi.....	Man	Mesentery and peritoneum	200 by 5	no	Absent
F. juncea.....	Man	Mesentery	100 by 5	no	Absent
F. immitis.....	Dog	Heart and large veins	280 by 5	no	Absent

That the retention of the embryos in the capillaries is the cause of their periodicity can easily be proved by the following simple experiment: Under normal conditions of temperature, etc., with a needle puncture the marginal vein of a dog infested with *F. immitis*, and in whose blood microfilariæ were found in a previous examination. Collect about 0.1 c.c. of the blood, and before it coagulates mix it with about 5 c.c. of a two per cent. acetic acid solution. After thoroughly shaking it to complete hemolysis, centrifugalize the mixture, decant the liquid, and collect the sediment with a pipet. Count the number of drops that make up the sediment and make fresh coverglass preparations, each one containing one drop of the sediment. Count the average number of embryos found in one drop (counting no less than two slides); multiply this number by the number of drops in the sediment, and this result, multiplied by ten, will give the number of embryos per cubic centimeter of blood.

Applying cold packing to the outer third of the ear, keeping the temperature of the part at 5° to 10° C. for from ten to fifteen minutes, and repeat the operation. Care should be taken, of course, to use the same ear and to collect the blood from the same vein, and as near as possible from the same point, avoiding undue pressure on the part. It will be found that the contraction of the capillaries by the action of cold has produced an appreciable retention of the embryos in the locality, as shown by the reduction in their number in the blood collected from the vein after the application of the ice-pack. The result of this experiment as performed by us was as follows:

Control blood: 50 microfilaria in 0.1 c.c. of blood
After ice pack: 17 microfilariæ in 0.1 c.c. of blood

That under normal conditions the retention of the microfilariæ in the capillaries is a constant phenomenon, can also be easily proved by counting the number of embryos found in an equal quantity of blood collected from the capillaries of the tip and from the marginal vein of the ear of the dog, or from the tip of the finger and vein of the arm in man, as the case may be, as is shown by the following results:

Filaria bancrofti

Peripheral blood: 150 microfilariæ in 0.1 c.c. of blood
Venous blood: 85 microfilariæ in 0.1 c.c. of blood

Filaria immitis

Peripheral blood: 45 microfilariæ in 0.1 c.c. of blood
Venous blood: 24 microfilariæ in 0.1 c.c. of blood

This retention of the microfilariæ in the capillaries also explains the phenomenon observed by Manson, who at autopsy found a larger

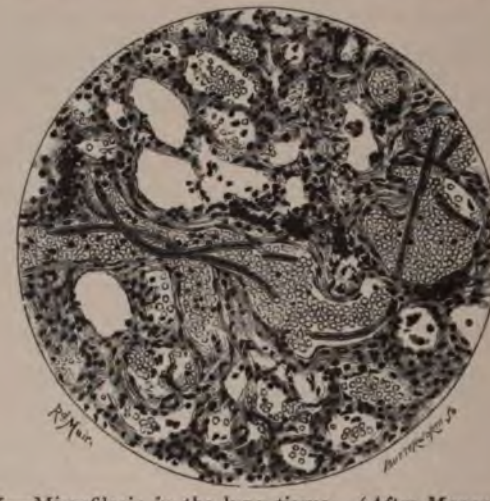


Fig. 227.—Microfilaria in the lung tissue. (*After Manson in Brumpt.*)

number of embryos in the blood from the lungs (Fig. 227) than in that from any of the other internal organs, as shown below. This, of course, is due to the proportionately large number of capillaries in the lung, and not to any specific attraction (organotropism) which these organs may have for the embryos. Finally, the retention of the embryos in the capillaries likewise explains the lesions of chronic filariasis, such as the occurrence of elephantiasis in dependent parts of the body, where the action of the heart is less vigorous (lower extremities, ear, etc.), and particularly in those parts, such as the scrotum and scalp, which, being provided with very tortuous arterioles and capillaries, favor the retention of the embryos, and the subsequent enlargement of elephantiasic lesions in these localities.

Another question that naturally suggests itself is why the microfilariæ of *F. loa*, which are the same size as those of *F. bancrofti*, and which like these, are provided with a sheath, show a reverse periodicity? This point will be discussed under *F. loa*, where it will be shown that identical conditions in the peripheral capillaries cause the retention of the embryos in this locality. Having previously shown that this retention in the capillaries is a constant finding under normal conditions, it may suffice, for the present, to say that, besides the action of the capillaries and size of the embryo, other factors, such as the habitat of the adult filaria, must be taken into consideration. It may be remembered, in passing, that *F. bancrofti*, besides inhabiting the lymphatics of the pelvis and other structures near the thoracic duct and the heart, has, in addition, a fixed habitat. *F. loa*, on the other hand, inhabits the subcutaneous tissue, distant from the heart, and as it possesses, in addition, a wandering habit, it cannot be expected, therefore, to show a precisely similar condition; nevertheless, the periodicity of *F. loa* can be explained on basis of the "Retention Theory," as will be shown further on.

Number of Microfilariæ in the Blood.—The number of microfilariæ in the blood varies from a few to several millions. Manson, basing his calculation upon the number of embryos found at night in preparations made from the peripheral blood, estimated that from 8000 to 10,000 embryos per cubic centimeter of blood are present, which would correspond to from 40,000,000 to 50,000,000 in the blood of an average sized person. It should be remembered, however, that Manson in his observation neglected the fact that under normal conditions, retention of the embryos takes place in the peripheral blood, and beside these figures are perhaps excessive, because the number of embryos present in the arterial and venous system at the

TABLE III.—ACETIC ACID CONCENTRATION METHOD

Hour of Collection	Number of Microfilariæ
12 Noon	30 per c.c. of blood
2 P. M.	15 per c.c. of blood
4 P. M.	10 per c.c. of blood
6 P. M.	35 per c.c. of blood
8 P. M.	50 per c.c. of blood
10 P. M.	640 per c.c. of blood
12 Midnight	760 per c.c. of blood
2 A. M.	5600 per c.c. of blood
4 A. M.	3400 per c.c. of blood
6 A. M.	2900 per c.c. of blood
8 A. M.	1000 per c.c. of blood
10 A. M.	110 per c.c. of blood
Total	14550 per c.c. of blood
Average	1212.5 per c.c. of blood

same time, or the average from a twenty-four-hour cycle, were not taken into consideration.

In investigations made along this line, from the average number in a twenty-four-hour cycle, the microfilariæ were found to number about 1200 per cubic centimeter of blood, or about 6,000,000 in the entire circulating blood, for a person of average weight (140 pounds), as is shown in Table III (page 415).

These figures are perhaps also too high, and the calculation made from the lowest counting obtained during the day, when the embryos are more or less evenly distributed in the blood (about 50,000), would probably represent the most approximate number in the circulating blood. Of course, the figures here given do not represent the total number present in the body, as many microfilariæ are constant at all times in their normal reservoir, in the lymphatics of the pelvis and abdomen, and in the blood capillaries in these regions, in the liver, kidneys, etc., and especially in the lungs.

Vitality of Microfilariæ.—It is a well-known fact that nematodes in general may live and show marked activity outside the host for some time. The adult filaria, when placed in salt solution, moves for several hours, and the microfilariæ live for several days *in vitro*, as was determined by us in the following experiment:

Fresh cover-glass preparations of a twenty-four-hour cycle were made from a case of *F. bancrofti*. Each preparation was sealed with paraffin to prevent evaporation, kept at room temperature, and the number of living microfilariæ on each slide counted at once and after one, two, three, and up to nine days. The result is shown in the following table:

TABLE IV.—VITALITY OF MICROFILARIÆ BANCROFTI *IN VITRO*: FRESH COVER-GLASS PREPARATIONS

Hour of Collection	Number of Living Microfilariæ Found									
	At Once	After 1 Day	After 2 Days	After 3 Days	After 4 Days	After 5 Days	After 6 Days	After 7 Days	After 8 Days	After 9 Days
9 P. M.	11	10	9	4	4	3	1	1	0	0
10 P. M.	25	18	10	9	8	4	3	1	0	0
12 M.	40	30	26	6	6	4	2	0	0	0
2 A. M.	50	48	36	24	24	9	4	2	1	0
4 A. M.	60	34	30	25	20	10	3	1	0	0
6 A. M.	50	50	45	22	6	3	3	0	0	0
8 A. M.	10	8	5	5	5	3	1	0	0	0
10 A. M.	3	2	1	0	0	0	0	0	0	0

From the table it will be seen that in those slides containing the larger number of embryos, living microfilariæ were found after the

eighth day, and if the observations were made with larger numbers of embryos it is probable that a thousand or more living microfilariæ would have been found for a period of ten days or longer. The viability of the embryos was determined by observing their motility, and those which, after an observation of from three to five minutes under the microscope, did not show any appreciable movement, were regarded as dead.

The viability of the embryos was much shorter (three to six days) when the slides were kept in an incubator at 38° C., or when exposed to the air or kept in a moist chamber at room temperature. Now if the microfilariæ live as long as from eight to ten days *in vitro*, it is natural to assume that under normal conditions they would live for a much longer time in the circulating blood or in the internal organs, as has been suggested by Bancroft.

Life History.—It is evident that though the microfilariæ may live for a month in the blood, observations have shown that they do not undergo any further development in the human body, but eventually die, degenerate, and disappear through the digestive action of the leukocytes, endothelial cells, and the digestive ferments of the tissue and the body, etc.,; hence for their further development the microfilariæ must be taken into the body of a mosquito, which acts as the intermediate host of the parasite.

The mosquitos known to act as the intermediate host of *F. bancrofti* are: *Culex fatigans, C. pipiens, Myzomyia rossi, Pyretophorus costalis, Panoplites africanus, Stegomyia calopus*, etc. It is probable that, besides the mosquitos, fleas, ticks, and bedbugs may also serve as secondary hosts. The mode of development is as follows:

The microfilaria enters the stomach of the mosquito with the blood, and leaves the sheath by rupturing it by means of the spine on the cephalic end. It now becomes free and very active, and piercing the wall of the stomach, finds its way into the body of the mosquito, eventually becoming lodged in the muscle of the thorax of the insect. In this new locality it undergoes development into a larva from in eight to fifteen days, according to the temperature and surrounding conditions, attaining a size of about 1.5 mm. in length by 0.2 mm. in width. At this stage the larva is provided with four lips, an alimentary canal, and a lobed tail (Figs. 228 and 229).

The larva now passes through the prothorax and head into the labium (esophageal pouch) and proboscis of the insect. When the mosquito bites, a thin membrane, known as Dutton's membrane, which lies between the labella and the chitinous skeleton of the labium, ruptures, and the larva is set free and penetrates the skin, either through the wound made by the mosquito or by piercing the epidermis, as is the case with ankylostoma larvæ (Lebredo). The future de-

velopment in man is not known, but the larvæ, after entering the body, are carried off by the lymphatic vessels or the blood, and become lodged in the lymphatics of the pelvis and other parts, where, in due course of time, they reach the adult stage and the cycle is repeated.

The duration of life of an adult filaria is not definitely known. From observations made by the author upon a case of *F. bancrofti*



FIG. 228.—Filaria bancrofti, larval stages as seen in the muscle of the mosquito. (*After Looss in Brumpt.*)

it was found to be about five years. This estimate was based upon the time when microfilariæ were first seen in the peripheral blood in a fresh cover-glass preparation, up to the time when none were found after repeated examinations of larger quantities of blood by the acetic acid concentration method, made at various times during the day and night. If, for instance, several months or perhaps a year were required for the adult females to generate a sufficient number of micro-



FIG. 229.—Filaria bancrofti mature larvæ in thoracic muscles and proboscis of mosquito. (*After Castellani and Chalmers in Chandler.*)

filariæ so that they could be detected in a cover-glass preparation (1 to 2 c. mm. of peripheral blood), and if, at the end of five years, embryos were still present, but in such small numbers that they could not be found (although about 3 c.c. of the patient's blood was examined), it may be assumed that some months or years more would be required for their complete disappearance. From what has been said it is evident that the life of a simple adult female is probably limited to from six to ten years.

It is unfortunate that data as to the duration of life of these parasites are lacking, since they would furnish a most reliable guide to the successful treatment of filariasis. For example: Given a case of filariasis, and assuming that the adult parasite lives only from six to ten years, by preventing a reinfection, either by change of habitat to non-infected districts or by other means, a favorable prognosis could be made with some degree of certainty, as during these years the parasite would, under normal conditions, die and disappear.

Mechanism of Transmission.—The infective stage in the life history of *F. bancrofti* is represented by the larval stage, as found in the mouth parts of the mosquito, the parasite being transmitted by the bite of this insect. The larva is deposited on the skin and enters the body either through the wound made by the mosquito or by actively piercing the skin.

Pathogenesis.—The presence of the parasite in man, at least for the first few years, may show no appreciable disturbance in the body. Often all symptoms except a mild degree of eosinophilia are entirely absent. In marked infection, *F. bancrofti* may give rise to a group of morbid changes known as filariasis.

In the early stages the disease may be manifested by periodic attacks of acute lymphangitis of one or both legs, lasting for one or two weeks, and accompanied by irregular fever. The microfilariæ may be found in the peripheral blood, especially at night.

The attack of lymphangitis gradually grows less severe, the affection taking a chronic course, and not uncommonly, at this stage, a unilateral or sometimes a bilateral adenitis of the inguinal lymphatic glands appears. This is followed by a moderate degree of edema of one or both legs, which, after several years, finally gives rise to a chronic dermocellulitis with marked enlargement of the parts known as elephantiasis.

The lesions of elephantiasis are not necessarily limited to the legs, but may also be seen in the mammæ, face, vulva, and other dependent parts of the body, or in those portions of the skin and subcutaneous tissues rich in capillaries where the vessels run a tortuous course, as in the scrotum and scalp.

It may be seen that the symptoms of filariasis, which are chiefly mechanical, are dependent on the habitat of the parasite. The adult males and females are coiled up together in the lymphatics of the abdomen, pelvis, scrotum, legs, hydrocele of the cord, epididymis, or testes, and are sometimes present in such numbers as to form masses that obstruct the lymphatic canals in this region, thus giving rise to attacks of lymphangitis and adenitis of the lymphatic glands of the groin and inguinal or femoral regions, and in some instances of the axilla. As the disease progresses the glands become enlarged and indurated,

and a degree of permanent edema of the subcutaneous tissues of the lower extremities appears, which gradually becomes more marked until, in typical cases, it attains an enormous size, with overhanging folds of edematous skin about the ankles, somewhat resembling the elephant's leg, hence the name, *elephantiasis*, given to this stage of the disease. Similar conditions may appear also in the scrotum, vulva, breast, arms, ears, scalp, etc. The terms filarial lymphangitis, filarial orchitis and hydrocele, filarial lymphangiectasis, and varicose lymphatic glands, respectively, have been applied to the various lesions produced. Not uncommonly a dilated lymph sinus or lacteal vessel may rupture into the urinary passages, the intestines, the tunica



FIG. 230.—Elephantiasis of the legs.



FIG. 231.—Elephantiasis of the scrotum.

vaginalis, or the peritoneum, giving rise to hematochyluria, chylous diarrhea, chylocele, and chylous ascites, respectively.

It may be added in this connection that elephantiasis, though commonly filaric in origin, as pointed out by Manson, may sometimes be induced by chronic conditions of the pelvis and groins (tumors, adenitis, thrombosis, etc.) which directly or indirectly interfere with the normal flow of lymph from the lower extremities. Also that climatic environments and occupational habit, as pointed out by Ruiz Arnau in his interesting observations on "Lymphectasia Tropicale Primitivé" are important predisposing factors to elephantiasis.

It is plausible that a filaric patient whose occupation compels him to stand most of the day, together with certain peculiar climatic factors of the tropics which to some extent predispose to a gradual loss of tonicity of the muscular walls of the lymphatics of the legs,

is more susceptible to elephantiasis than another patient living under different conditions.

It is a generally acknowledged fact at the present time that environmental conditions play a most important rôle in the symptomatology of diseases in general, and this is more especially true of parasitic diseases, the symptoms of which, as a rule, are atypical and not uncommonly entirely wanting. Filariasis may be said to be at the present a pandemic disease in so far as the modern means of transportation have disseminated filaric persons to all the civilized parts of the world and still elephantiasis, as before, remains a tropical complication of filariasis.

A symptom that may sometimes occur and that should not be overlooked is filarial hematuria, as observed by Dr. José M. Suarez. The author saw a case of periodic hematuria in an apparently healthy person. The urine was normal except for the presence of erythrocytes. Cystoscopic examination did not reveal any special lesion in the bladder, but on making an examination of the blood microfilariæ were found. The periodic attacks of hematuria are easily explained by the fact that the microfilariæ, being retained in the capillaries of the bladder, may eventually cause rupture of the blood-vessels, as is commonly the case with the eggs of *Schistosoma hematobium*, when lodged in the submucosa of this viscus. The occasional attacks of dysentery seen in filariasis may also be explained in a similar way.

The chronic cellulitis and hyperplasia of the skin commonly present in the advanced stages of elephantiasis may be aggravated by a secondary bacterial infection; moreover, since it is accompanied by a more or less well-marked round-cell infiltration and fibrosis of the subcutaneous tissue, ulceration and suppuration may occur.

Diagnosis.—Since the presence of *F. bancrofti* in the body does not necessarily imply the manifestation of any appreciable symptoms, and as lesions common to filariasis may be produced by other causes, such as tumors of the pelvis and abdomen, chronic adenitis, varicose veins, embolism of the veins or lymph-vessels, chronic lymphangitis, chronic cellulitis, climatic environment (Ruiz Arnau), etc., which directly or indirectly cause stagnation or obstruction to the flow of lymph, the diagnosis of filariasis is commonly based upon the finding of microfilariæ in the blood. It may be added, however, that the absence of the embryos in the blood does not necessarily exclude filariasis.

In elephantiasis, as is well known, the microfilariæ are not uncommonly absent in the blood, a finding that may be explained either by the fact that this disease may be caused by a variety of other conditions, as previously stated, or by the result of observations which showed that the elephantiasic lesions were a concomitant of the advanced stage of filariasis, when the adult female may have died, an occurrence

that, in the absence of reinfection, would account for the absence of microfilariæ in the blood.

It may be added here that since filariasis, even after it has been present for years, may not give rise to elephantiasis, the absence of microfilariæ from the blood in such cases does not necessarily exclude filariasis.

The foregoing facts show clearly that the diagnosis of filariasis is not, as is commonly believed, merely a question of the finding of microfilariæ in the peripheral blood. In suspected cases the diagnosis may be made, with a fair degree of certainty, by elimination, as may be illustrated by the following observations made on one of the author's cases:

A young man of twenty-three years was suffering from an attack of chronic adenitis of the left inguinal glands together with lymphangitis of the leg on the same side. When seen, he gave a history of similar attacks covering a period of six years. Repeated examinations of the blood failed to reveal the presence of any microfilariæ, but the differential count showed a considerable percentage of eosinophiles (8.5 per cent.). The absence of intestinal parasites or of any other metazoal infestation in the body strongly suggested a diagnosis of chronic filariasis, especially since a slight but permanent edema around the ankle, suggestive of a beginning elephantiasis, was already present. On further inquiry it was found that a diagnosis of filariasis had been made four years before, based on the finding of microfilariæ in the blood. The patient stated that at this time he had seen the filarial embryos in the preparations made of his own blood.

From what has been said it will be seen that a diagnosis of filariasis may be safely made in all cases of elephantiasis or in those cases that show symptoms or lesions common to filariasis, regardless of the absence of microfilariæ in the blood, provided the eosinophiles are in excess and other metazoal infestation can be eliminated as the result of examination of the feces, etc.

Search for the Parasite.—The laboratory diagnosis of filariasis is based chiefly on the finding of microfilariæ in the blood or chylous fluid, or upon discovering the adult filaria.

The Adult Filaria.—The adult filaria may not uncommonly be found in the cystic dilatations under the skin, lymphatics of the scrotum, arms, and legs, in hydroceles of the cord, epididymis, testicles, etc., or in other filarial lesions. At autopsy it may be found in the lymphatics of the pelvis. Male and female are usually found coiled together, and when placed in salt solution, will show active motion for hours. They appear as long, filiform organisms, somewhat whitish in color. The male measures about 40 mm. in length by 0. 1 mm. in width. The female measures 8 to 10 cm. in length by 0.2 to 0.3 mm. in width.

The Microfilaria.—The microfilaria is commonly found in the peripheral blood, but may also be detected in the chylous fluid, in lymph

from filarial lesions, or in the urine. The best results are obtained by centrifugalizing the suspected liquid and examining the sediment.

Search for Microfilariæ in the Blood.—If the examination is made at night, especially between the hours of midnight and 2 A. M., the embryos may easily be found in simple fresh cover-glass preparations; if, however, the blood is examined during the day, especially between the hours of 10 A. M. and 8 P. M., this method usually gives negative results. These negative results, as previously stated, are due not to the absence, but to the relatively small number of embryos present in the peripheral blood during those hours, as is proved by the fact that they are found to be present when a large amount of blood is examined (Table III, p. 415 and Table V, p. 424). The author has obtained very expedient and satisfactory results from using the acetic acid concentration method.

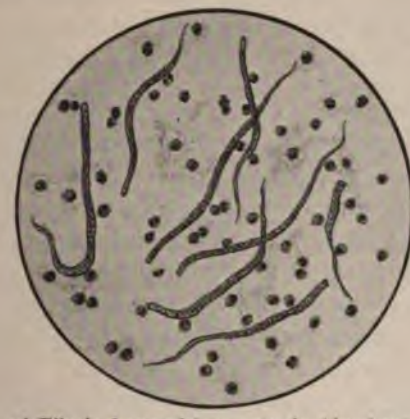


FIG. 232.—Embryos of Filaria bancrofti as seen in blood preparations made by the author by acetic acid concentration method under the low power of the microscope.

The Author's Acetic Acid Concentration Method.—This simple method consists in collecting a few drops—about 0.1 to 0.5 c.c.— of blood from the finger and placing it in about 10 c.c. of a 2 per cent. acetic acid solution. After thoroughly shaking to complete hemolysis, the mixture is centrifugalized. Fresh cover-glass preparations are made from the sediment and examined under the microscope. The advantage of this method over the common fresh cover-glass preparation method is illustrated in Table V.

Treatment.—The radical or specific treatment for filariasis has not yet been discovered. Thus far no drugs have been found that, directly or indirectly, exert any parasiticidal action upon the adult worm or the microfilariæ. The author has used salvarsan without any appreciable effects on the embryos. In the advanced stage of elephantiasis Castellani recommends the injection of thiosinamin or fibrolysin. The treatment of filariasis is merely symptomatic, and consists in the

TABLE V.—MICROFILARIA BANCROFTI IN THE PERIPHERAL BLOOD: TWENTY-FOUR-HOUR-CYCLE

Hour of Collection	Number of Embryos Found	
	By the common fresh blood cover-glass preparation method. Two slides examined	By the acetic acid concentration method in 0.1 c.c. of blood
12 Noon	0	5
2 P. M.	0	4
4 P. M.	0	3
6 P. M.	0	4
8 P. M.	0	10
10 P. M.	2	80
12 M.	26	260
2 A. M.	49	650
4 A. M.	57	520
6 A. M.	36	200
8 A. M.	12	110
10 A. M.	4	35

administration of tonics, iron, and arsenic for the secondary anemia, when present; rest and bandaging of the part for elephantiasis, etc. When the edema is very marked, tapping of the part and removal of the liquid give temporary relief, and may be repeated as often as required. The operation is very simple, and consists merely in leaving a cannula in the subcutaneous tissue for some time (over night or day), until a sufficient amount of lymph is withdrawn from the part. The surgical treatment, which consists in the removal of parts of the skin and subcutaneous tissues, may give temporary relief in some cases.

In the early stage of elephantiasis, when by chance microfilariæ are no longer found in the peripheral blood, the enucleation of the proximal lymphatic nodules of the groin, when indurated, and the deviation of the flow of lymph from the part to non-obstructed channels by anastomosis or otherwise, should be considered in the surgical treatment of the disease.

Prophylaxis.—The bite of mosquitos in localities where the disease is endemic should be avoided by the use of mosquito nets on the bed, and the screening of doors and windows. Mosquitos should be destroyed, preferably in the larval stage, by the application of petroleum to stagnant water, etc. Since mosquitos are more prone to bite at night, sleeping in the woods or remaining outdoors during the evening hours should be avoided.

It should also be remembered that a single infestation, limited perhaps to the introduction of only a few parasites into the body, may not give rise to any symptoms, and this probably explains the absence of any appreciable lesions in some cases of filariasis. If,

however, reinfestations should take place, there will naturally follow an increase in the number of filariæ and the manifestation of those symptoms common to the disease. In other words, not only the form, but the degree of infestation bears a direct relation to the severity of the lesions, and if, for obvious reasons, reinfection cannot be avoided, as in regions where the disease is endemic, the patient should be removed to a non-infested district, or, if possible, to a northern latitude, where in time (from four to ten years) the existing parasites will die and further complications will be avoided. By this course of procedure the author has seen two cases—one of infection by *F. bancrofti*, from the West Indies, and one of *F. loa*, from Africa—gradually get well, and a third case of infection by *F. bancrofti* greatly improve without any special treatment beyond removal to the northern part of this country.

2. Filaria loa (Guyot, 1778). *History.*—The occurrence of a filaria in the eye appears to have been known in Europe since the end of the sixteenth century, and Mongin, in 1770, described the presence of this nematode in the visual organ. Guyot, in 1778, introduced the term "loa" in European literature. Manson, in 1891, found the microfilaria in the blood of several negroes in Africa, and observing that, contrary to *F. bancrofti*, the embryos were found during the day, he gave it the name of *Microfilaria diurna*. The last-named author further suggested that it might be the embryo of *F. loa*. This hypothesis was later borne out by Penel, Prout, Henly, Brumpt, Wurtz, and Kerr. The adult inhabits the subcutaneous tissue in all parts of the body, and it is said to invade with preference those parts exposed to the light, such as the breasts, shoulders, face, conjunctiva, etc. So far as is known this filaria occurs only in man, and is restricted to the Congo region in Africa, which suggests that the intermediate host (probably an insect) has a limited geographic range.

Description.—The adult parasite is whitish in color, opalescent, and semitransparent. The tegument is smooth and covered with small elevations—papilla-like bosses—over the entire surface. These measure from 12 to 27μ in diameter and from 4 to 12μ in height. These papillæ are an important feature in differentiating this parasite from *F. bancrofti*. The body is pointed at both ends; the mouth part is unarmed and provided with two lips.

The *male* is thin, measuring 25 to 34 mm. in length (smaller than *F. bancrofti*) by 0.2 to 0.4 mm. in width. The head is truncated, and the neck but feebly differentiated from the remainder of the body. The posterior end is coiled and provided with two unequal spicules. There are three pairs of preanal and two pairs of postanal papillæ, and sometimes an additional pair of little tubercles may be seen on each side of the median line posteriorly.

The esophagus is short and without a bulb. It is continuous with a straight intestine that opens in the anus or cloaca at the posterior end. The excretory pore opens externally at about 0.6 mm. from the anterior end of the body.

The sexual organs consist of a single tubular testicle and vas deferens coiled on itself, which ends in the vesicula seminalis, situated near the base of the spicules.

The *female* is larger than the male, and measures from 45 to 65 mm. in length (smaller than *F. bancrofti*) by 300 to 500μ in width. The sexual organs consist of a pair of ovaries and two uterine tubes that lead into a single vagina and end in the vulva. The vulva is situated at about 2.5 mm. from the anterior extremity (Fig. 233.)

Habitat.—The adult filaria inhabits with preference the subcutaneous tissue. It has been found in the pericardium (Brumpt),



A B

FIG. 233.—Filaria loa cobbold, posterior extremity *A*, male; *B*, female. (*After Looss in Castellani and Chalmers.*)

but this location may be considered as anomalous. The parasite has no fixed locality, but wanders all over the body under the skin. It has been observed under the skin of the breast, shoulders, arms, fingers, face, eyelids, conjunctiva, mucosa of the tongue, etc. It not infrequently passes under the skin across the bridge of the nose, and may here easily be detected and felt with the finger. The parasite moves quickly, and gives rise to a temporary edema along its course ("Calabar swellings," "ambulant edema"). It may also cause itching, creeping sensations, etc. In its course the female deposits the embryos under the skin, and eventually, on being carried through the lymph-channels, they reach the heart and enter the peripheral circulation, where they can be found, especially during the day; hence the name, *Microfilaria diurna*, given by Manson.

Habitat and Morphology of the Embryos.—The microfilaria is found in the peripheral lymphatics and the blood-stream. In the peripheral

blood it is found especially during the day, between the hours of 10 A. M. and 4 P. M., being more abundant from 12 to 2 P. M. It is usually absent at night, especially between midnight and 2 A. M. This periodicity, therefore, is just the reverse of that of *F. bancrofti.*

Morphologically, the microfilariæ cannot be differentiated from the embryos of *F. bancrofti,* which, like the latter, have the same measurements and are covered by a sheath. According to Manson, the *microfilaria* of *F. loa* presents a somewhat less coiled appearance; the anterior end is more sharply bent, and the tip of the tail is not uncommonly folded on itself inside of the sheath.



FIG. 234.—Microfilaria loa. Unstained, in human blood.

Periodicity of the Microfilariæ.—As has been stated, the microfilariæ are especially found in the peripheral blood during the day, and are usually absent during the night. The condition is just the reverse of that of the microfilariœ of *F. bancrofti,* except that, according to some observers, the periodicity of *F. loa* is not so well defined. This point was studied by the author, with the results shown in Table VI.

Another point in the differentiation is the fact that, while in *F. bancrofti* the periodicity is reversed, if the patient changes his habit and sleeps during the day instead of at night, in *F. loa* the periodicity is unaffected under such conditions (Manson). In 1902 Brumpt observed that in Africa, where the negro laborers worked during the night and slept during the day, the microfilaria in the peripheral blood not only failed to show a reversion of the periodicity, but

TABLE VI.—FILARIA LOA: TWENTY-FOUR-HOUR CYCLE. PERIODICITY OF MICROFILARIA IN THE PERIPHERAL BLOOD. DRIED FILM PREPARATIONS

Hour of Collection	Number of Embryos in One Slide
6 P. M.	22
8 P. M.	15
10 P. M.	12
12 M.	10
2 A. M.	6
4 A. M.	3
6 A. M.	5
8 A. M.	10
10 A. M.	11
12 N.	27
2 P. M.	35
4 P. M.	30

that this was lost entirely, and this led him to believe in an infestation with *Filaria bourgi*. Finally, the same author observed an alteration or irregularity of the periodicity when the affection was associated with other pathologic conditions, such as sleeping sickness. From what has been said it may be concluded, therefore, that the periodicity of the embryos of *F. loa*, contrary to that of the embryos of *F. bancrofti*, is not a constant phenomenon and not uncommonly may be absent entirely.

Cause of Periodicity.—The cause of the periodicity of the microfilariæ of *F. loa* in the peripheral blood is explained also by the "Retention Theory," as was outlined in the case of *F. bancrofti* (p. 411). It will naturally be asked, "How is it that the same cause will produce two different effects?" Like the cause, the effects are, as a matter of fact, the same: the embryos of *F. loa*, like those of *F. bancrofti*, which are both of the same size and morphologically identical, are retained in the peripheral capillaries, the latter having a smaller diameter than the embryos. This has been demonstrated both by actual observation as well as experimentally, and has been explained in discussing the periodicity of *F. bancrofti;* the reversion or diurnal periodicity in *F. loa*, however, needs further elucidation.

Filaria bancrofti inhabits the lymphatics of the pelvis near the thoracic duct, and this naturally facilitates the constant passage of the embryos into the heart and their distribution to all parts of the body. That the increased action of the heart, external stimulation, muscular activity, etc., during the day, facilitate the constant passage of the embryos from the arterial to the venous system at this time, and that contrary effects at night cause retention of the embryos in the peripheral blood, have been demonstrated elsewhere. It has also been shown that this retention of the embryos is a constant phenomenon, since they are found in greater numbers at all hours of the day and night in the peripheral blood than in the proximal vein from the part (p. 414).

Conversely, *Filaria loa* has the habit of wandering about in the subcutaneous tissues. Its embryos are deposited distant from the heart, and as they are carried passively by the sluggish flow of the lymph in the lymph-channels in these localities, they are necessarily apt to be retained in the peripheral lymphatics during the night, when the action of the heart is less marked, and surface stimulations, muscular activity, nervous irritability, etc., are practically *nil*. This is especially the case during sleep, and would naturally explain the apparent absence of microfilariæ from the blood at this time; whereas conversely, with opposite conditions existing during the day, by facilitating the passage of the embryos from the lymphatics into the heart and the blood-stream, the greater number being found in the blood at these hours is accounted for.

A question that would naturally be asked is: "Why do not the embryos of *F. loa*, once in the blood-stream, behave the same and show a nocturnal periodicity just as do those of *F. bancrofti*?" This, of course, is easily answered: the embryos of *F. loa*, on entering the blood during the day, are gradually eliminated from the peripheral blood during night by being retained in the capillaries of some of the internal organs, especially the lungs, which may act as a reservoir, as was shown by Manson in *F. bancrofti*. That the lungs are especially adapted for retaining the embryos can easily be understood when considering the specialized capillary supply and spongy-like nature of these organs.

Finally, a further explanation as to the cause of certain peculiarities regarding the periodicity of *F. loa*, which the author ventures to suggest, is that for the manifestation of this diurnal periodicity it is essential that the infestation should be either very marked or of long standing, and have reached that stage in which the microfilariæ are present in sufficient numbers to be seen in the small amount of blood usually examined (1 to 2 mm.) by the fresh cover-glass preparation method. Of course, the embryos are present in the blood long before this stage is reached, as can easily be proved by examining a larger quantity of blood (0.1 to 0.5 c.c.) by the acetic acid concentration method. Furthermore, if, by the acetic acid method, the number of microfilariæ is counted from two equal amounts of blood, one taken from the tip of the finger and the other from the superficial veins of the forearm, it will be found that although the number of embryos in the capillaries of the finger is greater, the difference between the two specimens is slight. In other words, the result would show that the embryos of *F. loa* are distributed in the blood-stream more or less equally at all hours of the day and night. Of course the number of microfilariæ will be found to be greater in the capillaries, as is the case in *Filaria bancrofti*, but this discrepancy is less marked in *Filaria loa* (Rivas).

With these points in mind, it is easily understood that the diurnal periodicity is dependent upon an excess of microfilariæ entering the blood from the peripheral lymphatics, as well as from the lungs and other organs, during the course of the day, and their retention in the surface capillaries, this possibly also explains those obscure and irregular phenomena common to infestation with this parasite, namely:

1. Why in the certain regions of Africa in which the condition is endemic, and where infestation among adults is very high, children under five years of age do not show microfilariæ in their blood. These children may or may not be infested. If they are infested, the microfilariæ, being more or less equally distributed throughout the blood, are apt to be overlooked in the small amount of blood (1 to 2 mm.) that is usually examined. The examination of larger amounts of

blood by the acetic acid method would probably show the parasite. Infestation with *F. loa* may be divided into three stages: (1) "*Early aperiodic;*" (2) "*middle periodic;*" and (3) "*advanced aperiodic.*" The early aperiodic stage, corresponding to the time when the number of embryos is so small as to render them undetectable by the usual fresh cover-glass preparation, is probably of about five years' duration, and it is possible that this would explain the negative finding of microfilariæ in children under five years of age.

2. The lack of a sharp and constant periodicity in *F. loa.* This may be accounted for by the fact that the microfilariæ are deposited in the peripheral lymphatics, distant from the heart, and their entrance into the blood-stream depends largely upon the activity of the patient during the day or night hours, as the case may be.

3. The alteration or changes, but no reversion of the periodicity, when the patient changes the habit of sleep. This scarcely needs any further explanation than that already given. The periodicity, as stated, not being sharply defined, even under normal conditions, cannot be expected to show any marked variation by merely a change of habit of the patient, to sleeping during the day instead of at night.

4. Similar alteration or changes in the periodicity in cases complicated with sleeping sickness. The patient, being in a sleepy state most of the time, it is easily understood that after the embryos have been accumulated in sufficient numbers in the peripheral lymphatics, they will flow regularly into the heart and blood-stream, regardless of whether it is day or night. The author believes that, under such conditions, more or less similar changes will take place in *F. bancrofti.*

5. *Absence of Periodicity.*—This condition which corresponds to the third "advanced aperiodic" stage, is commonly seen in advanced cases or when the infestation is marked. Under such conditions the embryos in the peripheral lymphatics occur in such great numbers that they flow into the blood-stream in sufficient quantity at all hours of the day and night. It may be possible, too, that the number of microfilariæ entering the blood-stream during the day is so large that one part of them behave in the same way as the embryos of *F. bancrofti;* that is, they are retained in sufficient numbers in the peripheral capillaries at night so as to be found in the small amount of blood from the finger examined during this hour.

6. The relative scarcity with which the microfilariæ of *F. loa* are encountered in the peripheral blood, as compared with the numbers of *F. bancrofti.* This is due to the fact that, during the day, the same agencies that facilitate the passage of the embryos of *F. bancrofti* from the arterial to the venous system (heart action, surface stimulation, muscular activity, etc.), also facilitate the passage of the embryos of *F. loa* into the blood. In other words, these embryos, being

distributed more or less equally throughout the blood, only a relatively small number are retained in the peripheral capillaries. It is almost superfluous to add that the embryos are not found at night because of the relatively small number of them that pass from the peripheral lymphatics into the heart during the hours of rest, whereas those that have entered the blood-stream during the day have gradually been eliminated from the peripheral capillaries by being retained in the capillaries of the internal organs, as previously stated.

From what has been said it will be seen that the "Retention Theory" explains the periodicity of both *F. bancrofti* and *F. loa*. In both instances the cause of the periodicity is the same, namely, the retention of the microfilariæ in the peripheral capillaries. Certain variations or irregularities, of course, exist, but this could hardly be otherwise when the habitat of the adults is taken into consideration. Thus, while *F. bancrofti* lives in the lymphatics near the heart, the periodicity of the embryos may be said to depend upon only one cause —their retention in the surface capillaries. With *F. loa* this is not the case. The adult parasite wanders about in the subcutaneous tissue, distant from the heart, and the embryos are deposited there. The periodicity, therefore, is dependent upon two causes, namely: the entrance of the embryos, through the sluggish flow of lymph from the peripheral lymphatics, into the blood-stream, and their subsequent retention in the peripheral blood capillaries.

Life History.—Nothing definite is known regarding the further development of the embryos. Experiments made with mosquitos, *Glossinæ*, *Stomoxys*, and the mango-fly (*Chrysops dimidiatus*), have given negative results. The fact that *F. loa* is found only in the Congo region of Africa suggests that the evolution takes place in some insect common only to that country.

The duration of life of the adult filaria is not known, but it appears that the development of the parasite is much slower, and that it lives longer than *F. bancrofti*. Since the "early aperiodic stage" (when the embryos are not yet found in the peripheral blood) is probably about five years, and since, according to Brumpt's observation, the microfilariæ persist in the blood after the patient is removed to non-infected localities (away from the possibility of infection) for five years, the conclusion may be drawn that the life of the parasite is from ten to fifteen years.

Mechanism of Transmission.—This is not known, but, like *F. bancrofti*, the parasite is probably transmitted in the larval stage by the bite of an insect.

Pathogenesis.—The presence of *F. loa* in man does not usually give rise to any appreciable symptoms. The wandering habit of the adult parasite explains the absence of lymphangitis, chyluria, ele-

phantiasis, etc., common to *F. bancrofti*, which symptoms are due to blocking of the lymphatics and interference with the flow of the lymph. The passage of the worm under the skin may give rise to itching, creeping sensations, and temporary edema ("Calabar swelling" or "ambulant edema"). The localization of the parasite in the eye is not common (Brumpt), but when it lodges under the conjunctiva or in the deeper part of this organ, it may give rise to temporary conjunctivitis, neuralgic pains, etc.

Diagnosis.—Since the presence of *F. loa* does not usually give rise to any appreciable symptoms, the diagnosis is based upon the finding of the microfilariæ in the peripheral blood. The search for the embryos is made in the same way as has been described under *F. bancrofti*, *i.e.*, by the simple fresh cover-glass preparation. The blood should, when possible, be examined during the day, between the hours of 12 and 2 P.M. If the result is negative, or if the examination is made early in the morning, during the evening hours, or at night, a larger amount of blood should be examined by the acetic acid concentration method. The procedure as already described, is as follows: From five to ten drops of blood are collected in about 5 c.c. of a 2 per cent. solution of acetic acid, and after shaking until complete hemolysis has occurred, it is centrifugalized for a few minutes and the sediment examined. The microfilariæ are, of course, killed by the acid, but, like the microfilariæ of *F. bancrofti*, they are easily recognized.

Owing to the fact that the number of microfilariæ found in the peripheral blood is restricted to a very few or none, the diagnosis is sometimes not easily made, and cases in which the result is negative, but in which there is an excess of eosinophiles in the blood, in the absence of other metazoal infestation, together with the occasional occurrence of "Calabar swelling," should be regarded with suspicion.

As the periodicity of the microfilariæ in the peripheral blood is likely to be irregular or less marked, the number of embryos in a given quantity of blood during a twenty-four-hour cycle should be calculated, as shown in Table VI, p. 427, from which it will be seen that the larger number of embryos is found during the day between the hours of 2 and 4 P. M.

The fact should also be taken into consideration that in *F. loa*, as previously stated, the periodicity is often entirely absent, especially during *the early and the advanced aperiodic stages*, and since this may also occur in *F. bancrofti*, particularly in cases of long-standing infestation, the differential diagnosis may be made by the absence of elephantiasis, lymphangitis, chronic adenitis, chyluria, etc., lesions that are commonly produced by *F. bancrofti*.

Finally, the history of the case will sometimes reveal the fact that the adult parasite has been observed by the patient moving under

the skin of the arm, chest, face, etc., and a previous history of occasional attacks of ambulatory edema ("Calabar swelling") and itching and creeping sensations, when associated with an increase of the eosinophiles, should be regarded as suspicious.

Treatment.—While an infestation with *F. bancrofti* may be regarded as not amenable to treatment because of the habitat of the adult parasite in the internal lymphatics, *F. loa*, which lives in the subcutaneous tissue (where it may not uncommonly be observed under the skin), may easily be removed by a simple surgical operation, and if the infestation is limited to a few parasites, a radical cure can often be obtained.

To effect the removal of the worm it is important, first, to determine the location and direction of movement of the parasite. A short incision of the skin and subcutaneous tissue should quickly be made with a sharp knife, transversely to the direction in which the parasite is moving, and at a point a few millimeters to one centimeter ahead of it. Sterile or absorbent cotton should be placed at each side or at the distant lip of the wound, to remove any excess of blood. The wound should be kept as clean as possible, care being taken not unduly to touch or rub the lip of the wound. As soon as the parasite is seen to appear in one of the lips of the wound, the head should quickly be caught gently with a pair of forceps or hemostats and gradually be removed by gentle traction. *Care should be taken not to break the parasite while making the traction.* When situated under the conjunctiva the filaria may easily be extracted with a needle prick under it, and quickly withdrawn.

Prophylaxis.—As nothing is known regarding the development of the microfilariæ outside of the human body, no definite prophylactic measures can be recommended. It is well, however, on general principles, to avoid the bite of insects in localities in which the condition is endemic. A reinfection should be avoided, when possible, by removing the patient to non-infected regions, preferably to the northern latitudes, where in time (from six to ten years) the adult worm may eventually die.

3. **Filaria perstans** (Manson, 1891). *Description.*—The microfilaria of this parasite was discovered by Manson in 1891 in the blood of negroes in the Congo, and Daniels found the adult worm in British Guiana. At present the distribution of the parasite is confined to tropical Africa and British Guiana.

The adult worms are found free in the connective tissue at the base of the mesentery, around the pancreas, behind the abdominal aorta, and behind the pericardium and the suprarenal capsules. The body is filiform, cylindric, and somewhat tapered anteriorly.

The *male* worm is rarely found. It measures 45 mm. in length

by 0.06 mm. in width. The tail is curved and ends in a bifid prolongation of the cuticle, and is provided with a single spicule (Penel). Low found two spicules and four pairs of preanal and one of postanal papillæ. The cloaca is situated at about 120μ from the posterior end.

The *female* worm measures about 70 to 80 mm. in length by 0.12 mm. in width. It has a rounded head and a long neck. The mouth is small, and the alimentary canal does not appear to be divided into œsophagus and intestine. The anus is situated about 140μ from the tip of the tail. The uterus is double and ends in the vulva, which is situated about 0.6 mm. from the anterior extremity.

The Embryo.—The microfilaria, which has no sheath, is found in the blood. It is much smaller than the microfilaria of *F. loa*. Two types are recognized: one small, measuring 90 to 110μ in length by 4μ in width, and the other 160 to 600μ in length by 5 to 6μ in width. In stained preparations five clear spots may be recognized: (1) Cephalic; (2) oblique; (3) V-shaped; (4) central, and (5) caudal spots.

Periodicity.—There is no periodicity, as the microfilaria is found in the peripheral blood at all hours of the day and night.

Habitat.—As previously stated, the adult parasite lives free in the connective tissue of the mesentery, behind the abdominal aorta and pancreas, and behind the pericardium and around the kidney. The adult worm has apparently a wandering habit, as no appreciable lesions are seen in these localities.

Life History.—Nothing definite is known regarding the further development of the embryo outside of the blood. It is probable that, as in the case of *F. bancrofti*, this takes place in some insect. The experiments of Hodges, Low, and Brumpt with mosquitos, fleas, and lice gave negative results. Wellman and Feldham assert that development takes place in the tick.

Mechanism of Transmission.—Nothing is known as to the manner in which the parasite is transmitted.

The *pathogenesis* is nil.

4. **Filaria ozzardi** (Manson, 1895).—The microfilaria of this parasite was found by Manson in 1895 in the blood of man in the West Indies, and in 1898 Daniels discovered the adult female and the fragment of a male in the connective tissue behind the peritoneum at the root of the mesentery.

The *male* can hardly be said to be known, as only a fragment of the posterior end was found by Daniels. It was provided with a single spicule.

The *female* measures 65 to 80 mm. in length by 0.2 to 0.25 mm. in breadth. The tail is provided with a bulbous cuticular expansion. The anus is situated about 0.25 mm. from the tip of the tail, and the vulva about 0.7 mm. behind the cephalic end.

The *microfilaria* has no sheath and does not show periodicity. It measures 200 by 5μ.

The *life history* is unknown, and the *pathogenesis* is nil.

5. Filaria magalhæsi (Blanchard, 1895).—In 1887 the adult parasites, male and female, were found by Magalhæs in the heart of a child in Rio de Janeiro. The *male* measured 83 mm. in length by 0.2 to 0.4 mm. in breadth. The tail was provided with two spicules and four pairs of preanal and three pairs of postanal papillæ. The cloaca was situated about 0.11 mm. from the tip of the tail. The *female* measured 155 mm. in length by 0.6 to 0.8 mm. in breadth. The anus was situated about 0.13 mm. from the tip of the tail.

The *life history* and *pathogenesis* are unknown.

6. Filaria taniguchii (Penel, 1904). This parasite was found by Taniguchi in the lymphatic glands of man in Japan. Only the female and the microfilariæ are known. The *female* measures 68 mm. in length by 0.2 mm. in width. The anus is situated 0.23 mm. from the tip of the tail, and the vulva 1.3 mm. behind the mouth. The *microfilaria* measures about 164μ in length by 8μ in width. It is provided with a sheath and shows nocturnal periodicity.

The *life history* is unknown, and the *pathogenesis* is nil.

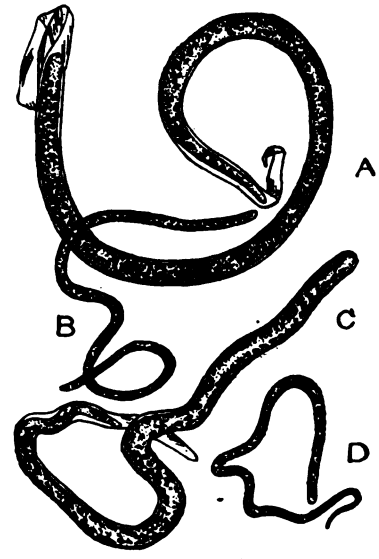


FIG. 235.—Comparison of microfilariæ. *A*, *mj*, bancrofti (large with sheath); *B*, *mf*, perstans (small, blunt tail, no sheath); *C*, *mj*, loa (large with sheath); *D*, *mf*, juncea (*demarquayi*) (small, sharp tail, with sheath). × 75. (*After Manson in Chandler.*)

7. Filaria juncea (Railliet and Neveu-Lemaire, 1908).—This parasite was discovered by Manson in the West Indies. The adult inhabits the mesentery; only the female and the microfilariæ are known. The *female* measures 65 to 81 mm. in length by 0.2 to 0.25 mm. in width. The anus is situated 230 to 250μ from the tip of the tail, and the vulva 710 to 760μ from the cephalic end. The *embryos* are not provided with a sheath, and have about the same measurements as the microfilariæ of *F. perstans;* like this, also, they show no periodicity.

The *life history* is unknown, and the *pathogenesis* is nil.

8. Filaria volvulus (Leuckart, 1893).—This parasite was found in man in West Africa in a tumor of the scalp. Labadie, Lagrave, Brumpt, and others have seen the worm in similar tumors in the arm,

and recently Fülleborn has studied the effect of the parasite in man. Males and females are found coiled together in the tumor, which may be of the size of a pea to that of a pigeon's egg (Fig. 236).

The *male* measures 30 to 35 mm. in length by about 130μ in breadth. The head is round and the mouth is unarmed. The cloaca is situated about 50μ from the tip of the tail and has three pairs of papillæ at the side and three pairs of postanal papillæ (Brumpt). The tail is provided with two unequal papillæ.

The *female* measures 60 to 70 mm. in length by about 360μ in breadth. The vulva is situated about 0.8 mm. from the anterior end.

The *microfilaria* has no sheath. It measures 250 to 300μ in length by 5 to 6μ in width, and has been found in the liquid obtained from the tumor, but not in the blood.

Habitat.—The adults and the microfilariæ, as previously stated, are found in the substance of the tumor which they produce under the skin. Microfilariæ are also found in the tumor, but have not yet been seen in the blood, probably because an insufficient amount of blood was examined.



FIG. 236.—Filaria volvulus as seen at the site of the lesion. (× 2 *after Brumpt.*)

Life History.—The life history is not known. Brumpt is inclined to believe that the further development of the embryo takes place in the tsetse-fly, and that this insect transmits the parasite.

Pathogenesis.—The parasite may give rise to attacks of lymphangitis, and sometimes to the development of acute and small subcutaneous tumors.

9. Rare or Doubtful Filariæ. Filaria powelli (Penel, 1904).—Found by Powell in India. The embryo measures 131 mm. by 3 to 5μ. Only the microfilaria has been found.

Filaria philippinensis (Ashburn and Craig, 1907).—This is differentiated from *F. bancrofti* by the absence of periodicity (?). Only the microfilaria has been found.

III. NEMATODES OF THE SUBCUTANEOUS TISSUE

Filaria (Dracunculus) medinensis (Linnæus, 1758). *History.*—This parasite commonly known as the "Guinea-worm," is endemic in India, Persia, Turkestan, Arabia, and tropical Africa. It is also found in some parts of South America, where it has been imported from Africa.

The worm has probably been known since the most ancient times, and was in all probability the fiery serpent mentioned by Moses, who is also said to have described the method of extracting it by twisting

the parasite on a stick. Galen named the disease caused by this parasite *dracontiasis*.

The anatomy of the parasite was studied by Bastian in 1863, and the infection of *Cyclops* with the larva was observed by Fedschenko in 1870. The transmission of the parasite experimentally into monkeys by feeding them with infected cyclops was carried out by Leiper in 1907, and his experiments were confirmed by Strassen.

Description.—The *female* worm is filiform in shape and whitish in color. It measures from 50 to 90 cm. in length by 0.5 to 1.7 mm. in its widest diameter. The mouth is terminal, and is provided with two lips and two lateral and four submedian papillæ. The alimentary canal is straight and complete in early life, but in the fully developed adult is atrophied near the tail and ends in a cecum without an anal opening. The vulva is situated close to the mouth and leads into the vagina, and a simple uterus and ovary all ar-

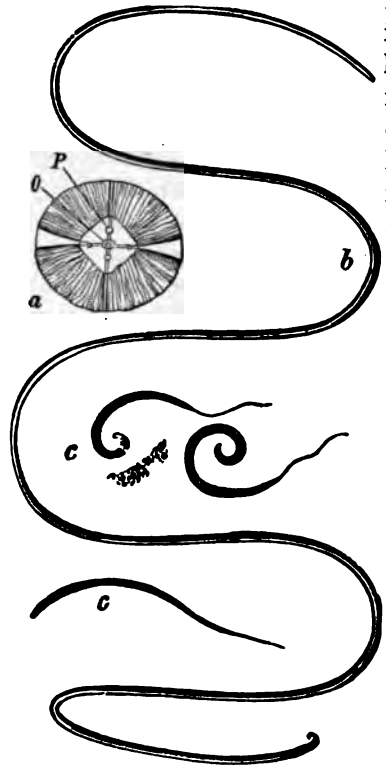


FIG. 237.—Filaria medinensis. *a*, front view of anterior extremity; *o*, mouth; *p*, papillæ; *b*, female reduced one half in size; *c*, embryos enlarged. (*After Bastian and Leuckart in Brumpt.*)



FIG. 238.—Filaria medinensis. Transverse section of an adult female showing the uterus containing many embryos. (*After Leuckart in Brumpt.*)

ranged in a tube that extends throughout the whole length of the body, complete the generative organs. When fully mature, the uterus is filled with embryos. The tail is rounded off and ends in a small bent hook.

The *male* is small. It measures about 2.5 to 4 cm. in length. The tail is provided with five pairs of postanal papillæ.

The *larvæ* are flat and have a pointed tail. They measure about 0.6 mm. in length by 17.5μ in breadth, and are provided with an alimentary canal, but no anus.

Habitat.—The adult filaria lives in the subcutaneous tissues of man. It may be found in the feet, arms, chest, shoulders, etc., in fact, any of the exposed parts of the body. The development of the worm has been observed experimentally in monkeys. The accidental occurrence of the parasite in oxen, horses, dogs, and cats has been reported by some observers. The larva is found free in the water. It enters the body of the *Cyclops* where it undergoes development and the changes preparatory to its successful entrance into man, which occurs through the medium of infected water.

Life History.—In early life the male and female live in the connective tissue of the mesentery. After copulation the male probably dies, for usually only the female is found under the skin; the gravid female then moves toward the subcutaneous tissue of the foot, leg, arm, or shoulder, as the case may be. The location of the parasite is usually determined by the presence of a small bulla on the skin which corresponds to the head of the worm, whereas the remainder of the body

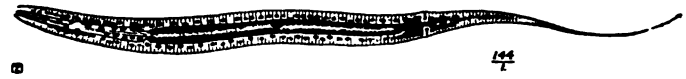


FIG. 239.—Larva of Filaria medinensis linnæus. (*After Looss, from Mense's Tropenkrankheiten, in Castellani and Chalmers.*)

appears in the form of an edematous and irregular cord under the skin. The bulla finally bursts, leaving a small hole, at the bottom of which is the vulva, and through which a portion of the uterine tube prolapses. A clear fluid escapes from the tube, which, if examined, is found to be full of larvæ.

The larvæ are actively motile. They escape and swim about freely in water, and either die or enter the alimentary canal of a cyclops, *C. coronatus* (Fig. 240), which is the intermediate host of the parasite.

In the body of the cyclops the larva undergoes development. The first molting takes place from about the seventh to the ninth day, and the second molting occurs about the tenth or eleventh day, after which developmental changes occur, and the larva reaches the infective stage at about the fourth week. By feeding a monkey with infected cyclops Leiper succeeded in demonstrating two females and one male in the animal, and from this it may be assumed that man is infected by swallowing infected cyclopides with the drinking water. In the stomach or the intestine the cyclops is digested, and the larva set free. It now penetrates the intestinal wall, and bores its way to the connec-

tive tissue of the mesentery, where it undergoes further development. After copulation the adult female migrates to the subcutaneous tissue, and after some time the larvæ are discharged in water, in the manner previously described, and the cycle is repeated.

Mechanism of Transmission.—The intermediate host of *F. medinensis* is the cyclops, *C. coronatus*, and the infective stage is represented by the larva as found in this crustacean four weeks after infection. Man is probably infested by the ingestion of infected cyclopides with the drinking water.

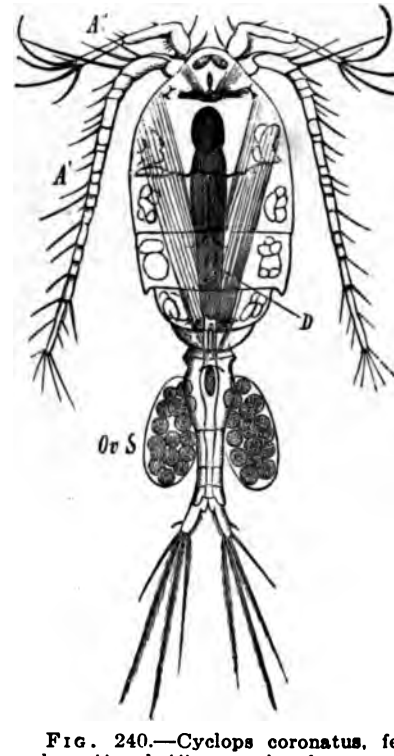


FIG. 240.—Cyclops coronatus, female. *A'* and *A''*, two pairs of antennæ; *D*, intestine; *Ovs*, ovarian sacs. (*After Blanchard in Brumpt.*)

Pathogenesis.—The presence of *Filaria medinensis* in man is the cause of a subcutaneous affection, commonly known as dracontiasis, which is manifested by pruritus, pain, edema, and at times ulceration and suppuration of the affected part. The location of the worm may be made out by the presence of an indurated and edematous cord under the skin, extending the entire length of the worm.

Diagnosis.—The diagnosis of dracontiasis is made without difficulty, as the presence of the parasite, as just stated, can easily be observed under the skin, taking the form of an indurated cord extending the entire length of the worm. Microscopic examination of the liquid which exudes from the ruptured bulla will reveal the presence of the larva.

Treatment.—The radical treatment consists in the extraction or destruction of the worm by the following methods:

1. The native mode of extraction, commonly used in certain parts of Africa and Asia, consists in catching the *head* of the worm as it protrudes through the opening in the skin. This is tied to a piece of wood and gradually twisted around it, a portion at a time, once or twice every day. About 3 or 4 cm. of the worm are thus extracted every day. Care should be taken not to break the parasite, since this may give rise to infection and suppuration.

2. The injection of mercury bichlorid 1 : 1000, recommended by



PLATE XII

Eustrongylus gigas; ♂, male and ♀, female in the pelvis of the kidney of a dog.

Emily. The method consists in injecting this antiseptic into the worm, when possible, or along the length of the swelling. The following day the parasite is gradually extracted, or a bandage is applied to the part to facilitate the absorption of the parasite.

3. The injection of chloroform has been recommended by Beelers, and injections of cocain and mercury bichlorid by Quinn.

4. Surgical treatment, which consists in the removal of the worm by operation.

Prophylaxis.—The prophylaxis consists in avoiding the use of unfiltered or unboiled water in localities where the worm is known to be endemic.

IV. NEMATODES OF THE KIDNEYS

Eustrongylus gigas (Rudolphi, 1802).—This nematode (Plate XII), commonly found in dogs, beeves, horses, and other animals, is a rare parasite of man, only nine cases being recorded. The worm, when fresh, is light reddish in color; the body is cylindric, and slightly attenuated at both ends. The cuticle is thin and finely striated. The mouth is hexagonal, and provided with six papillæ.

The *male* measures 14 to 40 cm. in length by 4 to 6 mm. in width. The caudal extremity ends in a collar-shaped bursa, somewhat oval in shape, and provided with three small papillæ. At the center of the bursa is the cloacal spicule, through the opening of which a single spicule may be seen. It measures 5 to 6 mm.

The *female* measures 20 cm. to 1 meter in length, by 5 to 12 mm. in width. The anus is terminal, and the vulva is situated about 50 to 70 mm. from the anterior end.

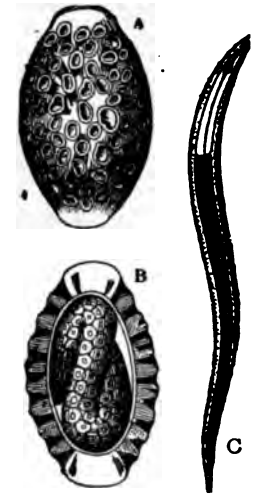


FIG. 241.—Eustrongylus gigas. *A* and *B*, eggs; *C*, free larva. (*After Balbiani in Brumpt.*)

The *eggs* (Fig. 241) are elliptic, thick shelled, and yellowish brown in color, and measure 65 to 70μ by 40 to 45μ. The shell of the egg is rough and presents numerous depressions, which give to the egg a mosaic appearance.

Habitat.—Both male and female are found together in the pelvis of the kidney or free in the peritoneal cavity. When in the kidney, they gradually give rise to distention of the pelvis and to atrophy and degeneration of the organ (Plate XII).

The *life history* is only partially known. The egg, when brought into contact with the water or moist soil, hatches a larva that is cylindric in shape and gradually tapered posteriorly. It measures about

240μ by 14μ. Further development is unknown, but it probably, like *Ankylostoma*, enters the host through the skin or through the mouth.

Pathogenesis.—The presence of this parasite in man is the cause of atrophy and degeneration of the kidney, painful micturition, hematuria, and renal colic. A bacterial infection may occur and give rise to suppuration of the genito-urinary tract.

Diagnosis.—The diagnosis is made without difficulty as the eggs are commonly found in the urine.

Treatment.—The radical treatment consists in the removal of the parasite by a surgical operation and also of the kidney, when advisable.

V. NEMATODES OF THE LUNGS

Metastrongylus apri (Gmelin, 1789).—This nematode, also called *Strongylus paradoxus* (Mehlis, 1831), is a parasite of the lungs of hogs,

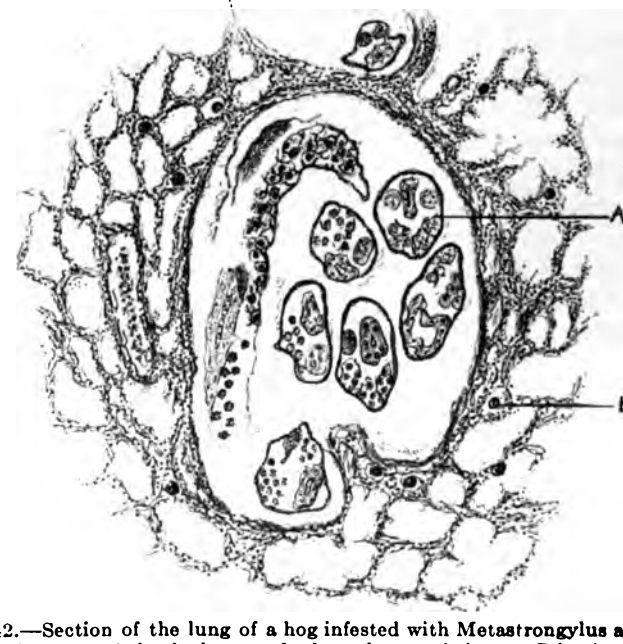


FIG 242.—Section of the lung of a hog infested with Metastrongylus apri showing sections of the worm *A*, in the lumen of a bronchus, and the ova *B* in the surrounding tissue.

and its occurrence in man is only occasional. The worm is short and slender, and white or brownish in color. The mouth is provided with six lips. The *male* measures 12 to 25 mm. in length. It has a bilobed bursa with five ribs in each lobe, and a pair of spicules about 4 mm. in length. The *female* measures 20 to 40 mm. in length; the anus

is subterminal, with the vulva anterior to it. The *eggs* are elliptic, measuring 50 to 100μ by 39 to 72μ; when oviposited, they contain an embryo.

Life History.—Only the embryo and larval development are known. The fact that the parasite inhabits the lungs and that it has sometimes been found in the intestine would suggest that its life history may be similar to that of *Ankylostoma*, although Leuckart failed to infect sheep by feeding them with sputum containing the embryos.

Pathogenesis.—The presence of this parasite in the lungs may give rise to bronchitis, pneumonia, abscesses of the lungs, and generalized secondary bacterial infection (Fig. 242).

VI. ERRATIC NEMATODES

Under the head of erratic nematodes will here be described: (1) The aberrant parasitic nematodes of man occasionally found in



FIG. 243.—Transverse section of Agamomarmis restiformis.

abnormal localities; that is, away from their normal habitat; (2) the parasitic nematodes of the lower animals, which, under certain conditions, may infect man; (3) the imperfectly known or immature forms of nematodes sometimes occurring in man; (4) the free living nematodes accidentally introduced into the human body.

1. **The Aberrant Parasitic Nematodes.**—Under this head may be considered any one of the well-known parasites of man which, owing either to a marked infestment or to a physicochemical change in the body, may inhabit organs other than the one commonly parasitized by the worm; thus, *Ascaris lumbricoides* may inhabit the peritoneal cavity, and has also been found in the large intestine, stomach, lung, etc. *Oxyuris vermicularis*, which normally inhabits the

small intestine when young and the rectum when adult, has been found in the appendix, stomach, esophagus, nose, etc., and in females it may parasitize the vagina and uterus. *Trichiuris*, which normally inhabits the cecum, has been found in the appendix and small intestine, etc. Most parasitic nematodes of man have occasionally been found in aberrant localities.

2. **Parasitic Nematodes of the Lower Animals.**—Certain parasites of the lower animals may, under some conditions, infect man. Thus, *Toxascaris canis* and *Toxascaris limbata*, which are parasites of the dog; *Trichostrongylus vitrinus*, a parasite of the sheep, *Gnathostoma siamense*, etc., have been known to occur in man.

3. **Imperfectly Known and Immature Nematodes.**—In this group may be placed several rare parasites that are occasionally found in man:

(1) *Agamofilaria georgiana* (Stiles, 1905), removed from a sore in the leg.

(2) *Agamofilaria oculi* (Von Nordman, 1832), found in the eye.

(3) *Filaria palpebralis* (Pace, 1867), found in a tumor of the upper eyelid.



FIG. 244.—Eggs of nematodes; *a*, Trichostrongylus instabilis; *b*, Ankylostoma duodenalis; *c*, Trichocephalus trichiuris; *d*, estrongyloides intestinalis; as seen in the uterus; *e*, Necator americanus; *f* and *g*, Ascaris lumbricoides after and before fertilization. (*After Manson in Brumpt.*)

(4) *Filaria labialis* (Pane, 1864), found in a pustule on the lip.

(5) *Filaria hominisoris* (Leidy, 1850), found in the mouth.

(6) *Filaria lymphatica* (Treutler, 1793), found in the bronchial lymphatic glands.

(7) *Agamomermis restiformis* (Leidy, 1880), found in the urethra.

4. **Free Living Nematodes.**—The best example of free living nematodes capable of infecting man is furnished by *Strongyloides intestinalis*, which, as previously described, has a saprozoic existence in the soil, but under certain conditions, in the larval stage, like *Ankylostoma*, it may enter the body of man and live as a parasite in the intestine. Several other species of free living nematodes that may accidentally enter the skin or the normal cavities of man and survive in these localities for a certain time have been described. Thus, *Anguillula aceti* has been found in the bladder; *Anguillulina putrefaciens*, in the stomach; *Leptodera pellio*, in papular eruptions of the skin; *Rhabditis niellyi* was found in the skin by Nielly, and is probably identical with *Leptodera pellio*, etc.

CLASSIFICATION OF EGGS OF NEMATHELMINTHES

Order	Differential Characters			Size in Microns	Species
Nematoda: Egg provided with a single-layered shell	Shell smooth	Thin	Oval, contains 2–4 cells	60×40	*Ankylostoma duodenalis*
			Oval, contains 2–8 cells	70×40	*Necator americanus*
			Oval, contains 4–8 cells	70×40	*Esophagostoma brumpti*
			Oval, contains 8–32 cells	80×48	*Trichostrongylus probolorus*
			Oval, contains 8–32 cells	83×43	*Trichostrongylus instabilis*
			Oval, contains 8–32 cells	87×48	*Trichostrongylus vitrinus*
			Oval, contains an embryo	54×32	*Strongyloides intestinalis*
			Oval, contains an embryo	80×55	*Metastrongylus apri*
		Thick	Flat on one side	50×23	*Oxyuris vermicularis*
			With one knob at each pole	55×25	*Trichiuris trichiurus*
	Shell ornamented	Thick	Oval, set with mammillary eminences; usually contains one cell	60×44	*Ascaris lumbricoides*
			Globular, contains one or more cells	75×65	*Toxascaris canis*
			Oval, set with mosaic-like depressions, one knob at each pole	66×44	*Eustrongylus gigas*
Acanthocephala: Eggs provided with a three-layered shell	Shell smooth	Thick	Contains an embryo provided with spicules or hooks on the surface	85×45 100×50	*Gigantorhynchus gigas* *G. moniliformis*

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CHAPTER XIX

ANNELIDA

Class Hirudinea.—Morphology and Structure.—Life History.—Pathogenesis.—Classification.—The Parasitic Leeches of Man: *Hirudo Medicinalis; H. troctina; Limnatis nilotica; Hemadipsa zeylanica; Hementaria officinalis; Placobdella catenigera.*

The annelids are metazoan invertebrates. They have a true celomic cavity and an elongated body, and are divided externally into a number of rings that correspond to the division of the internal parts into segments—*somites* or *metameres* (Fig. 246). Limbs are absent, but parapodia bearing *setæ* are present. The integument is soft and composed of few layers. The head consists of a *prostomium* united to one or more segments, and may be cirriferous or tentaculiferous. A vascular system distributing red blood is usually present. The nervous system is made up of a cerebral ganglion with double commissure and segmented ventral nerve cord. The excretory organs are in the form of metamerically arranged pairs of nephridia. The phylum is divided into several classes, of which only the *Hirudinea* or *Discophora* is of interest in human parasitology.

CLASS HIRUDINEA

The Hirudinea, commonly known as leeches (Fig. 245)are annelids having a sucking disk at one or at both ends. They are hermaphrodites and ametabolous (not subject to metamorphosis), and are found chiefly in fresh water, although some species are marine, whereas others live in moist soil. The distinctive characteristics that differentiate the Hirudinea from other annelids are:

1. The absence of bristles (except in *Acanthobdella*) and the presence of two suckers—one oral, used for prehension and the taking of food, and the other posterior and ventral, for attachment and locomotion.

2. The body is finely ringed, more rings than somites being present —three, five, or as many as fourteen rings may occur to a segment (Fig. 246). As in the earth-worm, at the time or reproduction certain segments may develop into a *clitellum* which secretes the egg cocoons.

3. The body is usually flattened in the dorsoventral plane, resembling in this respect the flat-worms.

Most of the leeches are free-living carnivora and feed on snails,

worms, fish, etc.; others are facultative parasites, feeding occasionally on the blood of vertebrates, whereas still others are true ectoparasites, subsisting exclusively on blood. These animals are of interest in human parasitology, first, because they are annoying ectoparasites; second, for the reason that, as endoparasites, may be a menace to the health or even to the life of a person; and third, because they may serve as carriers of pathogenic bacteria and protozoa—*e.g.*, the water leeches, as shown by Brumpt, are intermediate hosts of trypanosomes and other parasitic protozoa of the lower animals, and it is possible that they may also act as transmitters of similar parasites (Leishmania, Spirocheta, Trypanosomes, etc.).

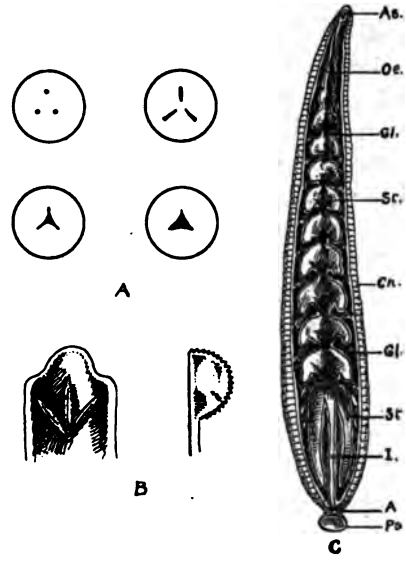


FIG. 245.—Diagram of a leech. *A*, different forms of the bite of a leech; *B*, sucker showing the jaws, one of which is magnified at the right; *C*, longitudinal section of the leech; *As*, anterior sucker; *E*, esophagus; *St*, stomach; *Cu*, cuticle; *I*, intestine; *A*, anus; *Ps*, posterior sucker; *Gl*, dermal glands. (*Slightly modified after Van Beneden.*)

Morphology and Structure.—Leeches may be studied without difficulty. The animal is killed by immersing it in boiling water or alcohol. On the surface the two suckers are readily seen. The body presents a large number of rings, and with the aid of a magnifying lens it will be seen, especially on the dorsal surface, that some of these rings are provided with papillæ (*sensillæ*) which are regularly arranged on every three, five, or seven rings. The name segment, *somite*, or *metamere* is applied to the system of rings occurring between the first ring with papillæ (inclusive) and the next ring with papillæ (exclusive), the first papilliferous ring being usually considered as the first ring of the *somite* (Fig. 246). More recent writers believe that a somite is determined by the limit of distribution of the nerves arising from a ganglion. These *somites* correspond to analogous segmentations of the internal parts of the animal, which is usually provided with an extensive celom. This celom is much reduced in the leeches, constituting a system of vascular sinuses.

On the ventral surface and along the middle of the body each somite is provided with two small orifices—the excretory or nephridial pores. On the median line of the ventral surface two orifices are seen: one anterior, the *male orifice*, provided with a penis in some genera or with an atrium producing spermatophores in others, and a posterior,

the *female orifice* (Fig. 246). Most species show a slight depression situated posterior to both genital openings, often marked by a change in color. This depression is produced by the presence in that locality of subcutaneous glands, and corresponds to the clitelligenous region or *clitellum* which secretes the egg cocoons during reproduction.

The Cuticle.—As in the trematodes, the cuticle is soft, and consists of epithelial cells and dermal glands. It is provided with bristles, cilia, or spines, except in *Acanthobdella*. Below the cuticle is a delicate subcuticular layer made up of a fine fibrillar structure (Fig. 245).

The Muscles.—As in the trematodes, there are three layers of muscles: The circular layer, situated below the subcuticle; the longitudinal muscles, arranged in long longitudinal plates below the circular layer; and the transverse muscles, which penetrate into the parenchyma. In addition, the suckers are provided with radial and meridional muscle-fibers that are particularly adapted for attachment and suction. The muscular system is of interest since it permits the contraction or elongation of the body, and gives the worm a characteristic "olive" shape in some species, or a relaxed, soft, elongated appearance in others.

The Digestive System.—The digestive tract is made up of a mouth, pharynx, esophagus, crop, stomach, intestines, and anus. The *mouth* may be armed or unarmed. When armed it is provided with three jaws—one dorsal and two ventrolateral, each with a thickened free edge notched with teeth (*Gnathobdellidæ*). When unarmed there may be only a strong, very muscular, protrudible proboscis, conic in shape, capable of perforating the skin, and serving for sucking (*Rhynchobdellidæ*).

On account of the differences in the structure of the mouth, the bite of the *Gnathobdellidæ* produces a triangular stellate wound, and that of the *Rhynchobdellidæ* produces a small opening (Fig. 245).

Opening into the mouth are the pharyngeal or salivary glands, which secrete an anticoagulant liquid. This substance can be extracted from the head of the leech, and is sold under the trade name "hirudin."

The *pharynx* is an oval sac provided with a strong muscular wall and radial muscles that, by alternate contraction and relaxation, dilate and contract the cavity, thus forming a sort of sucking pump. The pharynx is continuous with the *esophagus*, and leads into the *crop*, which is a thin-walled, straight tube having lateral diverticula.

Behind the crop is the *stomach*. This is relatively large, and is provided with numerous diverticula or *ceca*. The reaction of the stomach is acid, and the organ serves as a reservoir for the food (blood), which may remain unchanged or but slightly altered for some months.

Adjoining the stomach is a short *intestine*, which leads into the rectum and anus.

The excretory system consists of several nephridia that open along the middle of the body in the somites on each side, somewhat ventrally.

The vascular system usually contain red blood-cells, and in the *Gnathobdellidæ* consists of four longitudinal trunks—one dorsal, one ventral, and two lateral, connected by a system of capillaries.

The Parenchyma.—The parenchyma or supporting framework is made up of parenchymatous cells consisting of a nucleus and freely branched protoplasm. It fills the interstices between the internal organs, greatly reducing the internal cavity or *celom*, which is divided into several chambers, segments, or somites.

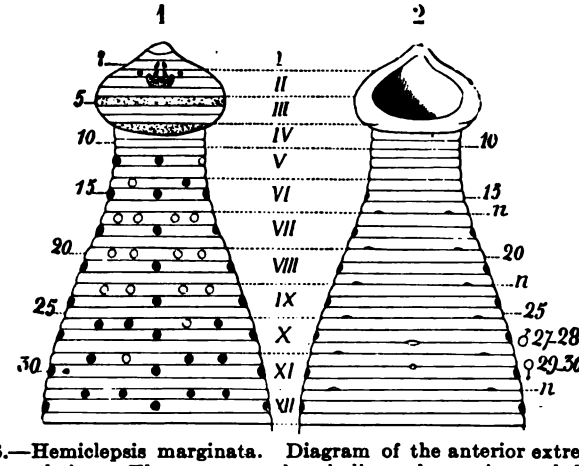


FIG. 246.—Hemiclepsis marginata. Diagram of the anterior extremity. 1, dorsal and 2, ventral view. The roman numbers indicate the somites and the arabic numbers the number of rings. *N*, nephridial pores; ♂, 27–28 male and ♀, 29–30 female genital pore. (*After Blanchard in Brumpt.*)

The nervous system consists of the brain and ventral cord, the latter often containing 23 ganglia. Nerve-fibers are given off to the eyes. The eyes, of which there are several, may be seen as small dark dots on the dorsal surface behind the anterior sucker. At each side of the ventral cord are the sexual organs.

The Reproductive Organs.—The leeches are hermaphroditic, and the reproductive organs are situated ventrally and at each side of the ventral nerve cord. The *male* sexual organs consist of several pairs of or numerous testes. In *Hirudo medicinalis* there are nine pairs of testes, the ducts of which unite to form a *vas deferens* on each side, which runs forward and, after coiling into the epididymis, empties into a single penis. The male genital pore opens ventrally anterior to the middle of the body and in front of the vulva. The *female* reproductive organs consist of two ovaries, which are situated in the space

CLASSIFICATION OF THE PARASITIC LEECHES OF MAN

Class	Order	Family	Differential Characters		Genus	Species
	I. *Acanthobdellidea:* Spines on anterior segments. Parasites of the lower animals.	I. *Herpobdellidæ:* Mouth without jaws, but with three folds.	Chiefly predaceous, parasites of the Lower animals.			
Hirudinea: Annelids with oval body. Dorsoventral flattening. Two suckers. Hermaphrodites. Reduced Celom. No parapodia.	II. *Arhynchobdellidea:* Body without spines. Mouth usually with jaws and without proboscis. Red blood. Predaceous or parasitic on man and other vertebrates	II. *Gnathobdellidæ:* Has the characteristics of the order. Number of eyes, usually 10.	Aquatic	Jaws provided with 50 to 100 teeth arranged in a single row. Number of rings, 102. Twenty-fourth to twenty-sixth somite with 2 or 3 rings each. Genital pore on the tenth somite.	Hirudo	*H. medicinalis* *H. troctina* *H. asiatica*
				Teeth less numerous. Number of rings, 103. Genital pore on the eleventh somite.	Macrobdella	*M. sestertia* *M. decora*
				Teeth rudimentary. Number of rings, 105 to 107. Sixth somite with 5 rings.	Whitmania	*W. ferox*
				Jaws with more than 100 teeth. Longitudinal groove on the inner surface of the upper lip of the anterior sucker.	Limnatis	*L. nilotica* *L. mysomel as* *L. granulosa*
				Teeth few and arranged in two rows. Twenty-third somite with 3 and twenty-fourth and twenty-sixth with 5 rings each.	Hemopis	*H. sanguisuga* *H. lacustra*
				Jaws provided with papillæ. Number of rings, 103 or 104. Sixth somite with 3 and twenty-third with 5 rings.	Limnobdella	*L. grandis* *L. australis* *L. mexicana*

		Terrestrial	A pair of tentacles on the sixth somite.		Xerobdella	
			Without tentacles	7 rings to a somite.	Planobdella	*P. quoyi* *P. molesta*
				6 rings to a somite.	Phytobdella	*Ph. meyeri* *Ph. moluccensis*
				5 rings to a somite.	Hemadipsa	*H. seylanica* *H. morsitans* *H. talagalla* *H. japonica*
				4 rings to a somite.	Philemon	*Ph. pungens* *Ph. grandidieri*
				3 rings to a somite.	Mesobdella	*M. gemmata*
III. *Rhynchobdellidea:* Mouth without jaws, but with proboscis. Colorless blood. Chiefly prey upon lower aquatic vertebrates, snails, and worms.	III. *Ichthyobdellidæ:* Anterior part narrow and distinct from the remainder of the body. Oval sucker large and expanded.		Large in size. Parasite of the shark and rays. Middle somites with 7 rings.		Pontobdella	
	IV. *Glossiphoniidæ.* Anterior sucker generally small and fused to the body; posterior sucker distinct. Body not divided into two regions.		Small in size or rudimentary. Chiefly parasitic on turtles and sometimes on man.		Placobdella	*P. catenigera*
			Parasite of man and lower animals. Large in size, each ring divided in two on the dorsal surface.		Hementaria	*H. officinalis*

between the epididymis and the first pair of testes; two oviducts (one from each ovary), which empty into a single vagina, and the vulva, which is situated behind the male genital pore.

Life History.—Like the trematodes, the leeches are oviparous, but unlike them they have no larval stage so that the development is ametabolous—that is, direct, and without metamorphosis as in the higher animals. The eggs, which are relatively few in number (50 to 80 in *Hemiclepsis marginata*), are fixed to a stone or piece of wood, and buried in the mud, or to the egg cocoons on the ventral surface of the parent. In time the eggs hatch and the young animals feed on the surrounding medium or attach themselves to a host and grow into adult leeches.

Leeches are essentially aquatic animals, but some species live in moist soil. In dry weather they remain hidden under stones, earth, etc. They appear to be very susceptible to external disturbances, and are readily aroused when man or animals approach their hiding places, and being ready to attack at once.

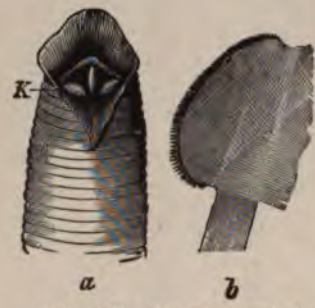


FIG. 247.—Hirudo medicinalis. *a*, Ventral view of the mouth showing the cutting jaws (*K*); *b*, a jaw enlarged showing the cutting teeth. (*After Leuckart in Brumpt.*)

The bite of the leech may not be painful and may even pass unnoticed until the flow of blood is observed. While biting, the leech keeps itself and the skin of its victim moist by means of the liquid excreted from the nephridium and dermal glands, and when gorged with blood it drops off. The wound, however, is likely to bleed profusely for some time on account of the salivary secretion, which prevents the coagulation of the blood. The blood is stored in the crop and in the ceca of the stomach, and only a small amount is used day by day for food.

Pathogenesis.—The pathogenic properties of leeches may be said to be nil, except for the loss of blood occasioned by the sucking of the leech and by the subsequent bleeding from the wound. The bite is apt to be the source of bacterial infection, and in some species, *e.g.*, *Hemadipsa ceylonica*, it is very prone to be followed by ulceration. The bite of *Hementaria officinalis*, common in Mexico, is said to cause drowsiness, buzzing in the ears, and a painful rash in man.

Classification.—The class Hirudinea may be divided into three orders: I. Acanthobdellidea; II. Arhynchobdellidea; III. Rhynchobdellidea.

ORDER I. *Acanthobdellidea.*—Characterized by the presence of spines on the surface of the body.

ORDER II. *Arhynchobdellidea.*—Marked by the presence of three jaws (*Gnathobdellidæ*)—one dorsal and two ventrolateral; the proboscis is absent; red blood-cells are present.

ORDER III. *Rhynchobdellidea.*—Characterized by the presence of a protrudible proboscis, the absence of jaws, and the presence of colorless blood.

Of these three orders, only the *Arhynchobdellidea* and *Rhynchobdellidea* are of interest in human parasitology, as they comprise the families *Gnathobdellidæ* and *Glossiphoniidæ* respectively, which include the parasitic species of man. The most important parasitic species may be described as follows:

ORDER *Arhynchobdellidæ*

FAMILY GNATHOBDELLIDÆ

Genus Hirudo (Linnæus, 1758).—Mandibles provided with a row of from 50 to 100 teeth; 24 somites, composed of 5 rings each. At present there are more than 20 species of this genus and of the genus *Macrobdella* that are known to attack man and the lower animals. In former years these leeches were used extensively for therapeutic purposes.



FIG. 248.—Hemadipsa zeylanica, natural size. (*Collect R. Blanchard after Brumpt.*)

1. **Hirudo medicinalis** (Linnæus, 1758).—This leech is from 8 to 13 cm. in length by 1 to 2 cm. in width. The dorsal surface is olive gray in color and presents six longitudinal bands. At each border, on the ventral surface there is a straight dark band.

Habitat.—This leech is common in Europe and Africa, and is usually found in stagnant water. In early life it is carnivorous and in the adult stage sucks blood. It attacks man and animals in general.

Pathogenesis.—The bite of the leech is not followed by any marked disturbance, except that the wound is predisposed to bacterial infection. Since the leech is aquatic, if it is accidentally swallowed with water it may lodge in the pharynx and give rise to grave symptoms.

2. **Hirudo troctina** (Linnæus, 1816).—This leech is from 8 to 20 cm. in length by 1 to 1.5 cm. in width. The dorsal surface is bright green in color and presents six rows of small black spots surrounded by an orange-colored zone resembling the spots of the trout; hence the name. The marginal bands on the ventral surface are arranged in zigzag fashion. It is found in the north of Africa and in Europe, and is the medicinal leech of England, France, Spain, and Algeria.

Genus Limnatis (Moquin-Tandon, 1826).—Mandibles provided with more than 100 teeth. This genus contains species resembling the *Hirudo*, some of which are of very large size, measuring over 40

cm. in length (Brumpt). Three species are important, since they may become lodged in the pharynx and upper respiratory passages and give rise to serious symptoms. These are: *Limnatis nilotica, L. mysomelas,* and *L. granulosa.*

1. Limnatis nilotica (Savigny, 1820).—This leech measures 8 to 10 cm. in length and 1 to 1.5 cm. in width. It is variable in color, but the ventral surface usually presents a deeper coloration than the dorsal. The body is soft, and it does not contract to the "olive" shape, as does hirudo. The leech inhabits the lakes and rivers of northern Africa. In the early stage of development it may easily be swallowed with the water and become lodged in the pharynx of



A *B*

FIG. 249.—Hementuria officinalis. *A*, ventral and *B*, side view. (*Collection R. Blanchard after Brumpt.*)

man. The adult is not uncommonly found in the normal cavities of animals, in which it may give rise to grave symptoms.

Genus Hæmadipsa (Tennent, 1861).—These are territorial leeches, small in size, measuring 2 to 3 cm. in length. They have five pairs of eyes, five rings to a somite, and are chiefly tropical.

Hæmadipsa zeylanica (de Blainville, 1827).—This leech (Fig. 248) is very common in Ceylon. It measures 2 to 3 cm. in length, and is a common parasite of man and animals. Its bite is painful and the wound may bleed for a long time.

ORDER *Rhynchobdellidea*

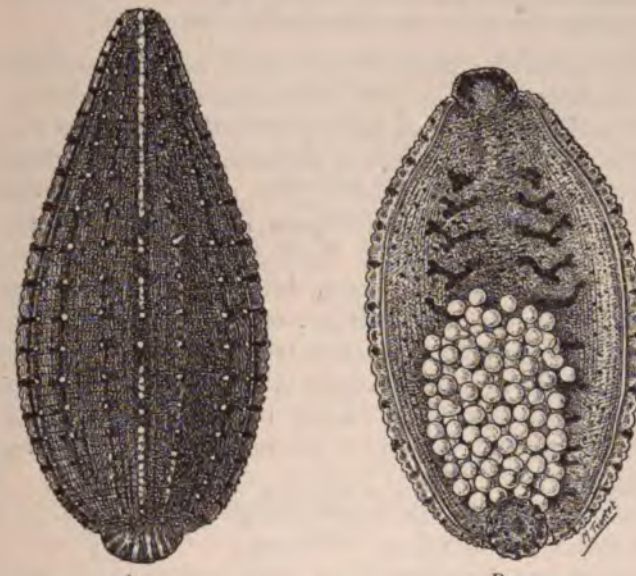
FAMILY GLOSSIPHONIIDÆ

Genus Hementaria (de Filippi, 1849).—Middle somites composed of six rings. The body is usually corrugated. Only a few species are found that attack man.

Hementaria officinalis (de Filippi, 1849).—This leech (Fig. 249) is common in Mexico and Central America, where it is used for therapeutic purposes. The wound made by the bite is the shape of a single hole. It is said that the bite sometimes gives rise to drowsiness, painful rash and general disturbance.

Genus Placobdella (Moquin-Tandon, 1846).

Placobdella catenigera.—This species is smaller than the foregoing, measuring 2 to 3 cm. in length. It attacks man and mammals. The bite is not painful, but the wound is prone to bleed for a long time. This leech is found in Europe.



A *B*

FIG. 250.—Placobdella catenigera. *A*, ventral and *B*, dorsal view. (× 2 *after Brumpt.*)

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CHAPTER XX

ARTHROPODA

GENERAL CONSIDERATION OF ARTHROPODS

Morphology and Structure.—Geographic Distribution and Habitat.—Parasitic Types.—Pathogenesis.—Classification: Protoarthropoda; Euarthropoda; Diplopoda; Chilopoda; Crustacea; Arachnida; Insecta (Hexapoda).

The arthropods are bilaterally symmetric invertebrates, with well-developed celomic cavities and heteronomously segmented bodies. They are non-ciliated animals, having articulated limbs and a ladder-like nervous system. The brain is supplemented by a ventral chain of ganglia arranged metamerically. The sexes are divided and are commonly oviparous. The arthropods include the spiders, crabs, insects, and myriapods, which, together with the annelids, were included by Cuvier in his subkingdom Articulata. This order contains the vast majority—about four-fifths—of the members of the animal kingdom, more than 300,000 species being known. The arthropods and the annelids have many features in common, but the former are differentiated from the latter chiefly by: (1) The character of the segmentation of the body, and (2) the presence of hollow segmented appendages.

In treating the arthropods the author has followed to a large extent the excellent entomology of Folsom.

Morphology and Structure.—The body regions in the arthropods (Fig. 251) may be divided into: (1) The head; (2) the thorax; and (3) the abdomen; and, in addition, (4) the jointed appendages that give the name to the group. Fewer regions may be made out when the head and thorax unite (cephalothorax) (Fig. 252), or, again, the number of segments may be increased by a division of the abdomen into the abdomen proper and the post-abdomen (Fig. 253). Finally in many arthropods (mites or acarina) all differentiation into somites disappears because the internal fusion of parts has obliterated the evidence of external segmentation (Fig. 254).

In most arthropods the anterior pairs of primary appendages are brought together to form the mouth parts and sense organs, and the segments to which they belong become fused into a single anterior mass—the head—in which the original segmentation is obliterated. As a rule, one segment overlaps the one next behind, but the head, although not a single segment, does not overlap the prothorax in a

typical manner, but is usually received into that segment, thus allowing freedom of movement to the head and affording protection for the articulation itself. In some arthropods almost the entire surface of the head is occupied by the eyes, as in Odonata (dragon-fly), Diptera (house-fly), etc., whereas in the larva of the latter "maggot," the head is rudimentary. In adult arthropods the head is commonly oval or globular in shape, and often bears appendages of various kinds, some of which are plainly adaptive, whereas others are merely ornamental.

The Appendages.—The appendages of arthropods are highly developed parapodia, taking the form of hollow joints provided with an intrinsic musculature. There is but one pair to each somite, and these belong to the ventral surface. Accordingly, if more than one pair of appendages are seen in any region without any external signs of segmentation, this region contains as many segments as it does pairs of appendages (Savigny). Thus the unsegmented head of an insect consists of at least four segments and the

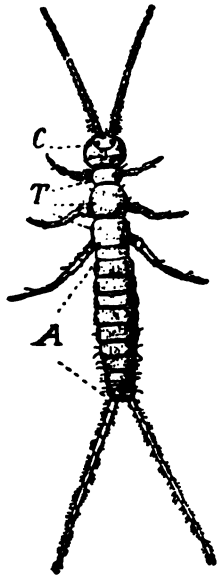


Fig. 251.

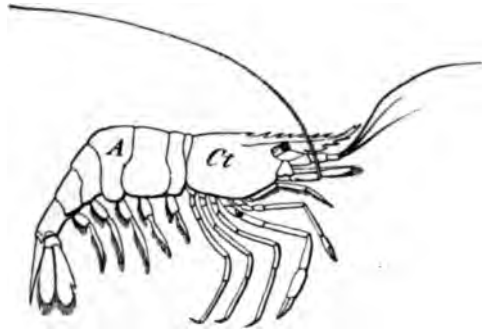


Fig. 252.

Fig. 251.—Campodea staphylinus. *A*, abdomen; *T*, thorax; *C*, head. (*After Huxley in Hertwig.*)

Fig. 252.—Palæmon serratus showing fusion of the head and thorax into the cephalothorax *ct*; *A*, abdomen. (*After Ludwig-Leunis in Hertwig.*)

cephalothorax of a lobster is made up of thirteen segments, for one bears four and the other thirteen pairs of appendages. This is demonstrated by ontogeny, for while in the embryo the somites are usually visible, it does not follow that each somite in the adult should show appendages, since they may have disappeared during growth without leaving any trace.

According to their function, the appendages may be divided into the following classes: Tactile, suctorial, locomotor, pleopoda, and winged appendages.

The *tactile appendages*, or antennæ (Figs. 255 and 256) of which

there are rarely more than one pair (two pairs in Crustacea and none in Arachnida), are situated upon the head, near or between the eyes, and usually consist of several segments that vary in form. In some insects the male is easily differentiated from the female by the great size and more complex structure of the antennæ. Although the function of the antennæ is chiefly tactile, it may also be olfactory (beetles, moths), auditory (mosquitos), etc. The suctorial, locomotor, pleopoda, and winged appendages are described in Chapter XXII, under Insecta.

The Nervous System.—Arthropods have a ladder-like nervous system (Fig. 257). This is composed of: (1) A dorsal brain or *supra-esophageal ganglion;* (2) a ventral cephalic or *sub-esophageal ganglion*, connected by a pair of nerve-cords, and *esophageal commissure*, between which passes the esophagus; and (3) a ventral chain of *thoracic*

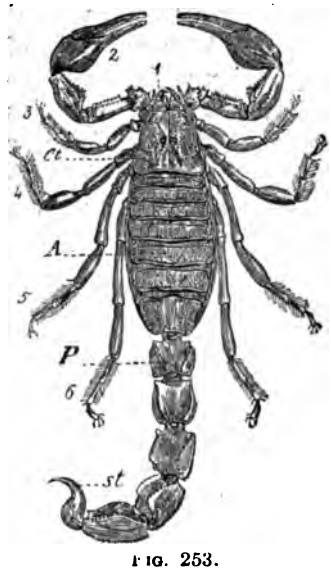


FIG. 253.

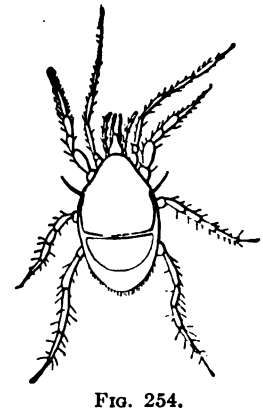


FIG. 254.

FIG. 253.—Androctonus australis showing division of the abdomen into abdomen proper, *A*, and post abdomen, *P;* 1, cheliceræ; 2, pedipali; 3 and 6, legs. (*After Hertwig.*)

FIG. 254.—Gamasus coleopteratorum showing almost an obliteration of external segmentation. (*After Taschenberg in Hertwig.*)

and *abdominal ganglia*, all connected by nerve-cords. The ventral chain should contain as many pairs of ganglia as there are somites, but this is not the case, except in the embryo. There is a tendency, rather, toward fusion of the ganglia, especially of those somites that unite, the extreme being reached in spiders and crabs, where the whole ventral chain forms a large ganglionic mass. The brain innervates the eye and antennæ; the sub-esophageal ganglion, the mouth parts; and the thoracic and abdominal ganglia, the appendages of their respective segments.

Sense Organs.—Of the sense organs, the best known are the eyes (Fig. 258) of which there are two types: *simple* and *compound*. The compound eye, or eye proper, is oval, triangular, convex, or hemispheric in shape, and not uncommonly the eye of the male is larger than that of the female. Superficially, a compound eye is divided into minute areas or *facets*, which, though spheric, are generally more or less hexagonal as the result of mutual pressure on one another. The number of these facets is often enormous: thus the housefly has 4000 to each eye; a butterfly (*Papilio*), 17,000, and one of the beetles (*Mordella*), 25,000. Structurally, each facet consists of a *cornea*, *crystalline lens*, *vitreous body*, *retina*, *iris*, *pigment*, and *fibers* of the *optic nerve*, all arranged from an elongated element called an *ommatidium* (Fig. 260). Many Crustacea and Insecta have compound eyes, but these organs are not present in Arachnida and Myriapoda.

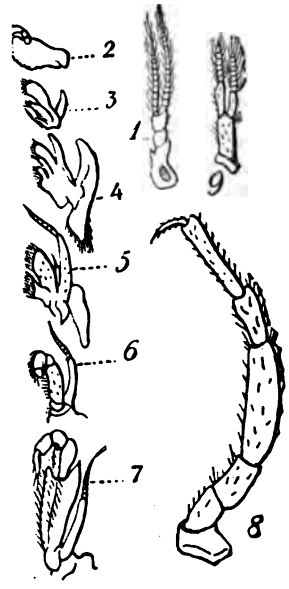


FIG. 255.—Appendages of the crayfish. 1, first antenna; 2, mandible; 3 and 4, first and second maxillæ; 5, 6 and 7, maxilipeds; 8, walking legs; 9, pleopoda. (*After Hertwig.*)

The simple eyes or *ocelli* (Fig. 261) are very small, and appear as tiny polished lenses, either lateral or dorsal in position, between the compound eyes, and correspond structurally more or less to an *ommatidium* of the compound eye. There are ordinarily three ocelli in insects, occurring on or near the vertex, arranged in the form of a triangle. In other arthropods their number varies from two to eight.

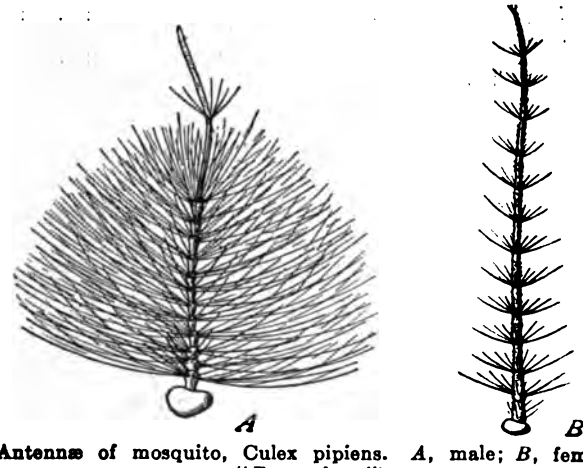


FIG. 256.—Antennæ of mosquito, Culex pipiens. *A*, male; *B*, female. (*Folsom "Entomology."*)

Next in importance are the *tactile organs*, which consist of tactile hairs and antennæ; together with the organs concerned in the sense of hearing, taste, smell, etc.

Digestive System.—In primitive types the intestinal tract is formed by a single tube extending along the axis of the body, and consisting of *fore-gut*, *mid-gut*, and *hind-gut* (Fig. 262). There are, however, many departures from these primitive conditions, and in the most highly specialized insects the tract is made up of: (1) ***Fore intestine*** or *stomodeum:* Mouth, pharynx, crop, proventricle (gizzard), and cardiac valve; (2) *midintestine* or *mesenteron:* Ventriculus or stomach; (3) *hind intestine* or *proctodeum*: Pyloric valve, ileum, colon, rectum, and

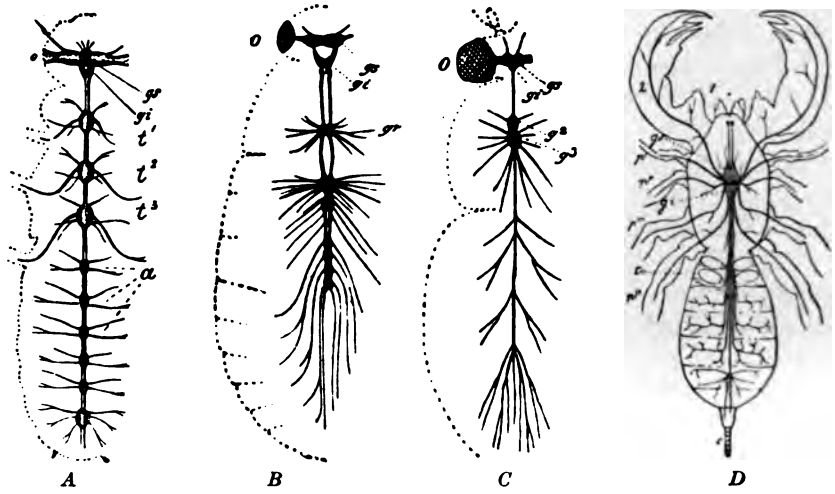


FIG. 257.—Diagram showing different degree of concentration of the ventral cord in Arthropodes from a chain of several ganglions in termite to few in the fly and a single ganglion in spiders and crabs. *A*, termite; *B*, water beetle; *C*, fly; *D*, teliphonid; *a*, abdomen; g^2, g^3, ganglia of ventral cord; gi, infra-esophageal ganglion; gs, supra-esophageal ganglion; *O*, eye; *p'–p'v*, walking feet; *tr*, lung hooks; 1, cheliceræ; 2, pedipalpus. (*After Lespes; B, C and D after Blanchard in Hertwig.*)

anus. Ciliated cells do not occur—arthropods in general are non-ciliated animals.

Excretory System.—The excretory organs show wide variations in the different groups: True nephridia are present in *Peripatus;* shell glands and antennæ glands in Crustacea, and Malpighian tubules in insects and arachnids.

The Malpighian tubules or kidneys are long, slender, blind tubes, opening into the intestine behind the stomach, and formed by evaginations of the proctodeum. Their number ranges from four to six to as many as 150, depending on the species. They are richly supplied with tracheæ, and are composed of polygonal cells set on a delicate

basement membrane and surrounded by a peritoneal layer of connective tissue. The cells are provided with a very large nucleus, which is often branched. The free ends of these tubes float in the celomic cavity. Their function is analogous to that of the kidney in vertebrates; they contain uric acid and its derivatives.

In addition, various spaces in the body are filled by a material made up of connective-tissue cells richly supplied with fat, in which uric acid also is present; this has given rise to the belief that they serve as permanent storage cells for the deposit of excrementitious products, or as temporary reservoirs before these are eliminated by the excretory organs. (For further details concerning the anatomy, development, embryology, life history, etc., of Arthropoda see Chapter XXII, under the head of Insecta.)

Geographic Distribution and Habitat.—Insects and arthropods in general



Fig. 258.

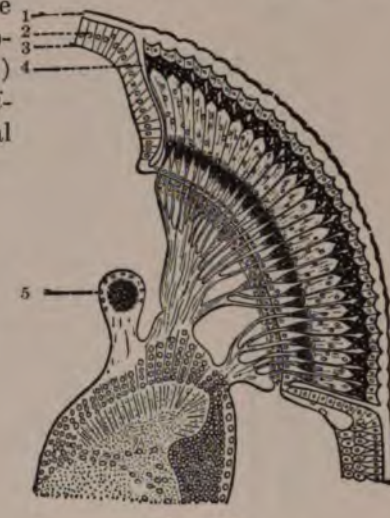


Fig. 259.

Fig. 258.—Head of a drone bee showing the large faceted eyes and between them three ocelli. (*After Swammerdam in Hertwig.*)

Fig. 259.—Section of compound eye of Forficula. 1, cuticular, producing the cornea of many lenses over the eye; 2, epidermis, which in the eye forms the ommantidia; 3, basal membrane; 4, reentrant chitinous fold (sclerotic); 5, rudimentary larval eye. (*After Carrière in Hertwig.*)

have been found in every latitude inhabited by man. Butterflies and mosquitos occur beyond the Polar latitudes, the former in Lat. 83° N. and the latter in Lat. 72° N. The general distribution of animals presents such peculiarities that naturalists have divided the earth into several zones, each of which has a characteristic fauna and flora. Five zones are generally recognized: The *Holarctic, Neotropic, Ethiopian, Oriental,* and *Australian* (J. W. Folsom, "Entomology"). These faunal realms, are not, of course, marked off by distinct boundaries, since the fauna overlap one another. Many insects are cosmopolitan in nature, but some species are not;

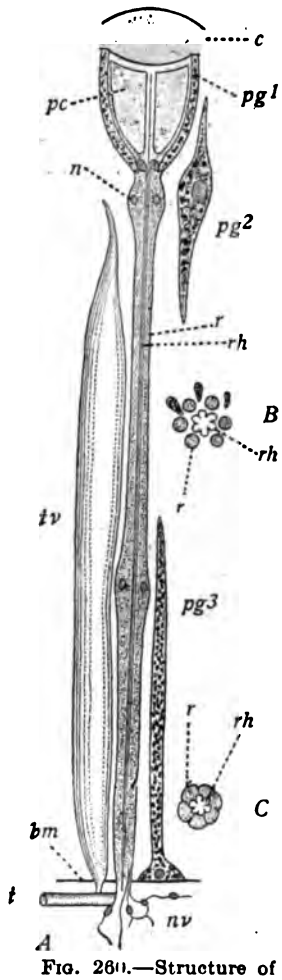


FIG. 260.—Structure of an ommatidium of Calliphora vomitoria. *A*, radial section (chiefly); *B*, transverse section through middle region; *C*, transverse section through basal region; *bm*, basement membrane; *c*, cornea; *n*, nucleus; *ns*, nerve fibrillæ; *pc*, pseudocone; pg^1, pg^2, cells containing iris pigment; pg^3, cell containing retinal pigment; *r*, one of the six retinal cells which compose the retinula; *rh*, rhabdom, composed of six rhabdomeres; *t*, trachea; *tv*, tracheal vesicle. (*After Hickson in Folsom.*)

for example, *Stegomyia calopus*, the yellow fever mosquito, is circumtropical, and *Glossina palpalis*, the tsetse fly of sleeping sickness, is found only in West and Central Africa and in Arabia.

As to habitat, insects may be divided into two classes—*aquatic* and *terrestrial*. These do not, however, form separate groups in a systematic classification, since an adult terrestrial insect may have an aquatic larva. The aquatic insects, as a rule, live in fresh water, but a few are marine, and even under certain conditions of environment a larva that commonly lives in fresh water, such as that of *Anopheles*, may survive and develop in salt water (Rivas).

Parasitic Types.—Most arthropods are free living, but many species exist as external parasites on the higher animals and man, whereas but a few are true internal parasites. A number of insects, however, (Diptera and Hymenoptera), may undergo larval development as internal parasites living on other insects or higher animals and on man. These larvæ, in general, are apodous; the body is fleshy and compact, and the head is sometimes reduced to the merest rudiment.

Arthropods may be divided into—(1) Free living and (2) parasitic; the latter may be subdivided into—(*a*) periodic parasites (flies, mosquitos, ticks, bedbugs, etc.) and (*b*) permanent parasites (*Sarcoptes*, *Pediculus*, etc.). The free living forms, of which the house-fly is an example, may be carriers of bacterial diseases; the periodic parasites, such as the mosquitos, bedbugs, ticks, fleas, etc., may be transmitters of protozoan or bacterial diseases, and the permanent parasites, such as lice and acarina, are themselves the causes of certain diseases in man and animals, although they may also occasionally serve as carriers or transmitters of microörganisms.

Pathogenesis.—Arthropods are rarely the cause of important diseases in man. Their

chief importance in human parasitology arises from the fact that they act either as direct carriers or as secondary hosts of several bacteria and protozoa respectively which cause disease in man and animals.

With the exception of the *Myriapods*, which are merely accidental parasites of man, and of the *Crustacea*, among which only one, *Cyclops coronatus*, acts as the intermediate host of *Filaria medinensis*, the *Arachnida* and *Hexapoda* embrace the species that are of importance in human parasitology.

Thus among the *Acarina*, *Sarcoptes scabiei*, besides being a permanent parasite, probably transmits *Bacillus leprœ*. As to the ticks,

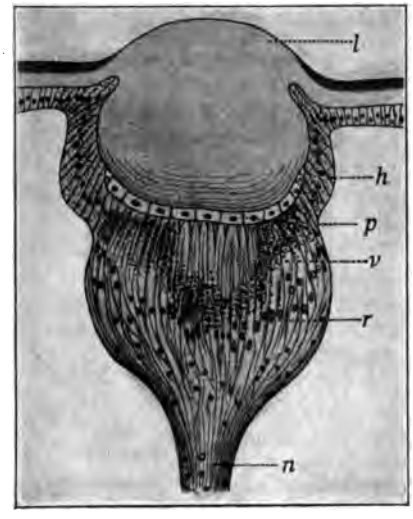


FIG. 261.—Median ocellus of honey bee (*Apis mellifera*), in sagittal section. *h*, Hypodermis; *l*, lens; *n*, nerve; *p*, iris pigment; *r*, retinal cells; *v*, vitreous body. (*After Redikorsew in Folsom.*)

Ornithodoros moubata transmits relapsing fever; *Euripicephalus appendiculatus*, Texas fever; *Dermacentor venustus*, Rocky Mountain fever, etc.

Among the *Hemiptera*, the lice, besides being permanent parasites, transmit typhus fever, and probably trypanosomes and other blood parasites; *Cimex lectularius* transmits relapsing fever; *C. rotundatus*, Oriental sore; *Lamus* (*Conorhinus*) *megistus*, *Trypanosoma cruzi*.

Among the *Diptera*, *Anopheles* transmits the malarial parasite; *Xenopsylla cheopis*, *Bacillus pestis;* the *Tabanidæ*, trypanosomes of animals; *Glossina palpalis*, sleeping sickness, and the house-fly is responsible for the transmission of several bacterial and probably protozoal diseases; Culex, Filaria, etc.

Classification.—Latreille divided the arthropods into four classes: *Crustacea, Myriapoda, Arachnida,* and *Insecta.* Somewhat later Moseley's discovery, that *Peripatus* (Fig. 263) possessed trachæ, led to the

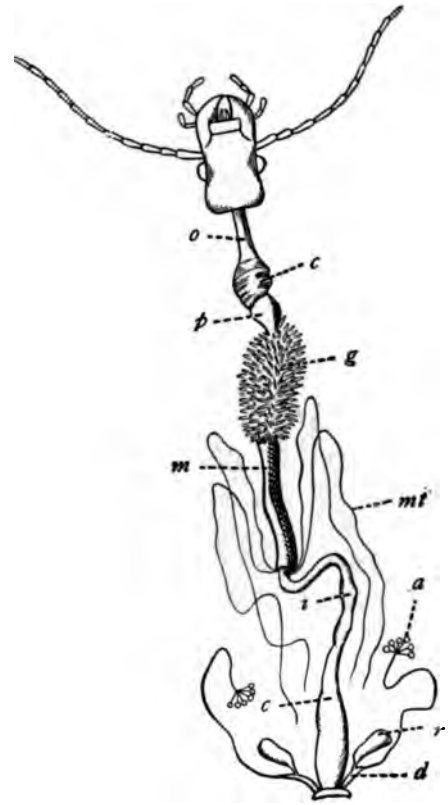


FIG. 262.—Digestive system of a beetle (*Carabus*). *a*, anal gland; *c*, (of fore gut), crop; *c* (of hind gut), colon, merging into rectum; *d*, evacuating duct of anal gland; *g*, gastric ceca; *i*, ileum; *m*, mid intestine; *mt*, Malpighian tubes; *o*, esophagus; *p*, proventriculus; *r*, reservoir. (*After Kolbe in Folsom.*)

creation of a new class, *Protracheata,* and to the grouping of arthropods into *Branchiata* and *Tracheata.* Further research showed that this



FIG. 263. –Peripatus capensis. Natural size. (*After Moseley in Folsom.*)

division was not a good one. Lankester divides the group into: (1) *Protarthropoda* and (2) *Euarthropoda.*

PROTARTHROPODA.—Primitive, terrestrial, worm-like arthropods, resembling the annelids. Body unsegmented externally; one pair of antennæ and a pair of jaws. Legs numerous, paired, and imperfectly segmented. Respiration through tracheæ, with stigmata all over the body. Numerous nephridia arranged segmentally in pairs, as in the annelids. The order contains a single class, *Malacopoda*, and a single genus, *Peripatus*, with several species, none of which, however, has been found to be a parasite of man.

EUARTHROPODA.—Arthropoda, with a distinctly segmented body; respiration through branchiæ or tracheæ (terrestrial or aquatic). It contains five classes: I. Diplopoda; II. Chilopoda; III. Crustacea; IV. Arachnida; V. Insecta (Hexapoda).

Class I. Diplopoda.—Terrestrial; body cylindric and divided into two regions: head and body. Numerous segments, most of which are double and bear two pairs of limbs. Eyes simple; antennæ short. Mouth parts consist of a pair of mandibles and a paired plate (*gnathochilarium*). Genital pore on second anterior segment. Example: *Spirobolus* (Fig. 264).



FIG. 264.—A diplopod (*Spirobolus marginatus*). Natural size. (*After Folsom.*)



FIG. 265.—A centipede (*Scolopendra heros*). About two-thirds the maximum length. (*After Folsom.*)

Class II. Chilopoda.—Terrestrial. Two regions: head and body, numerous segments, bearing a six- or seven-jointed limb on each side. Eyes simple and numerous. A pair of mandibles and two pairs of maxillæ; genital pore posterior, on the preanal segment. Example: *Scolopendra* (Fig. 265).

Class III. Crustacea.—Commonly aquatic. Head and thorax united into a cephalothorax. Two pairs of antennæ. Brachial or cutaneous respiration. Example: *Cyclops.*

Class IV. Arachnida.—Terrestrial. Commonly two regions: cephalothorax and abdomen. Cephalothorax bears two pairs of oral appendages and four pairs of legs. Abdomen without limbs. Pulmonary, tracheal, or cutaneous respiration. Examples: *Spiders, ticks,* etc.

Class V. Insecta (Hexapoda).—Usually terrestrial. Body divided into three regions: head, thorax, and abdomen. One pair of compound eyes; one pair of antennæ. Three pairs of mouth parts: mandibles, maxillæ, and labia, and in addition, a hypopharynx or tongue. Three pairs of thoracic legs, (hence the name, *Hexapoda*). One or two pairs of wings. Usually ten abdominal segments. Tracheal respiration. Examples: *Bedbug, louse, house-fly, mosquito, flea,* etc.

Of these five classes, the first three—*Diplopoda, Chilopoda,* and *Crustacea*—are of no importance in human parasitology with the exception of one crustacean, *Cyclops coronatus,* which serves as the intermediate host and transmitter of *Filaria medinensis.* The *Arachnida* and *Insecta* contain all the species known to be parasitic of man.

CLASSIFICATION OF ARTHROPODA

Differential Characters	Class
Terrestrial. Vermiform. Unsegmented externally. One pair of antennæ and jaws. Numerous legs, paired and short. Numerous nephridia	I. Melacopoda
Terrestrial. Two regions: head and body. Numerous segments, mostly bearing two pairs of limbs. Antennæ short	II. Diplopoda
Terrestrial. Two regions: head and body. Numerous segments, bearing one pair of six- or seven-jointed limbs	III. Chilopoda
Aquatic. Head and thorax united into a cephalothorax. Two pairs of antennæ	IV. Crustacea
Terrestrial. Two regions: cephalothorax and abdomen. Abdomen without limbs; no antennæ	V. Arachnida
Terrestrial. Three regions: head, thorax, and abdomen. One pair of antennæ. Six limbs. Three pairs of mouth parts and a hypopharynx	VI. Insecta

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CHAPTER XXI

CLASS ARACHNIDA

Order Linguatulida: *Linguatula rhinaria; Porocephalus armillatus; P. moniliformis.*—Order *Acarina.* I. Demodicoidea: *Demodex folliculorum;* II. Sarcoptoidea: *Sarcoptes scabiei.*—III. Ixodoidæ—The Ticks.—Family Ixodidæ.—Family Argasidæ.—Family Trombidiidæ.—Family Tarsonemidæ.

The Arachnida are terrestrial arthropods, having pulmonary (scorpions, spiders), tracheal, or cutaneous respiration. The body is generally formed of two parts: the *cephalothorax*, containing the mouth parts and four pairs of legs, and the *abdomen.* This class comprises several orders, of which only two—(A) The *Linguatulida* and (B) the *Acarina*, are parasites of man.

A. ORDER LINGUATULIDA

The members of the order Linguatulida are parasitic Arachnida, having a ringed, elongated, and vermiform body. The mouth is terminal or subterminal, and provided with a chitinous ring and two pairs of chitinous hooks on each side. Legs are absent. The anus is subterminal. The sexes are divided. The genital pore in the female opens in front of the anus, and in the male it opens ventrally, near the anterior end of the abdomen.

Life History.—The female lives in the nasal cavities of dogs, wolves, foxes, horses, goats, and sometimes of man. It discharges the eggs in the ground. These, on being taken into the stomach or intestine of an intermediate host—a herbivorous animal, rabbit, sheep, etc. —hatch in the stomach a four-legged larva that penetrates the intestinal wall and migrates to the liver, where it encysts, undergoes metamorphosis, and becomes a nymph. It may now leave the cyst, migrate to the intestine or bronchus, and reach the nasal cavity, where host, or, on being swallowed by a carnivorous animal—a dog—it is set free in the stomach, travels to the mouth, and nasal cavities of the dog, where it becomes an adult.

The order Linguatulida comprises two genera, *Linguatula* and *Porocephalus*, the following parasitic species being known:

1. **Linguatula rhinaria (serrata,** Fig. 266) (Fröhlich, 1789).—The male is white, and is 18 to 20 mm. in length by 3 mm. in width. The female is grayish in color, and 8 to 10 cm. in length by 8 to 10 mm.

in the anterior part, and about 2 mm. in the posterior part, in width. The eggs measure 90 by 70μ.

Habitat.—The adults inhabit the nasal cavities of dogs, horses, goats, etc., and at times those of man.

Life History.—The eggs are laid in the nasal cavities, and are expelled by sneezing. Falling on the grass, they are taken into the alimentary tract of a herbivorous animal, where they hatch into embryos. These measure about 130 by 60μ, have two pairs of legs, and are provided with an anterior perforating apparatus, a stylet, and two hooks, by means of which they bore through the walls of the intestine into the liver, lungs, mesenteric ganglion, etc., becoming encysted in about eight weeks, and then losing all their appendages. After several moltings, a larva develops, which grows to a length of about 6 to 8 mm. In this stage, when swallowed by a carnivorous animal, such as a dog, it is set free in the stomach, from which organ it travels to the mouth and nasal cavity, where it again molts and becomes an adult. Copulation takes place in about six to eight weeks after infection, eggs are discharged, and the cycle is repeated.



FIG. 266.—Linguatula serrata, natural size. (*After Brumpt.*)

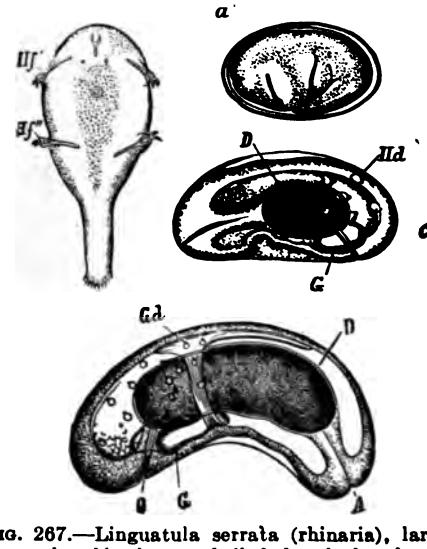


FIG. 267.—Linguatula serrata (rhinaria), larval forms. *a*, embryo enclosed in the egg shell; *b*, hatched embryo provided with two pairs of hooked legs (*Hf'* and *Hf''*); *C*, larva in the liver of rabbit; *Cr*, ganglion; *D*, intestine; *Hd*, cutaneous gland; *d*, older larva; *O*, mouth; *A*, anus; *Gd*, genital gland. (*After Leuckart in Brumpt.*)

Pathogenesis.—Cases in which this species was found in man at autopsy did not show any appreciable symptoms during life. Both the larvæ and the adult forms have been found in man.

2. **Porocephalus armillatus** (Wyman, 1848).—The body is cylindric, somewhat flattened anteriorly, and contains from 16 to 20 rings. The *female* (Fig. 268) measures 9 to 12 cm. in length and 5 to 9 mm. in width. The mouth is provided with two papillæ and two pairs of hooks. The genital opening is situated in front of the anus. The *male* (Fig. 268) measures 3 to 4.5 cm. in length by 3 to 4 mm. in width. The genital opening is situated in the middle of the ventral surface. The *larva* or nymph (Fig. 269) is found encysted in the organs of the host. It resembles the adult in the number of rings present.

Habitat.—The adult inhabits the trachea and lungs of the African python, *P. sebæ*, *P. regius*, etc. The larval forms are found in the liver, kidneys, lungs, etc., of monkeys, lions, and occasionally in those of man.

Life History.—Unknown; probably resembles that of *Linguatula rhinaria*, the only difference being in the hosts.



FIG. 268.



FIG. 269.

FIG. 268.—Porocephalus armillatus; ♀, female; ♂, male. Natural size. (*After Sambon in Chandler.*)

FIG. 269.—Nymph of Porocephalus armillatus Wyman encysted in the liver. (*After Sambon in Castellani and Chalmers.*)

Pathogenesis.—Unknown; it may be the cause of pneumonia, peritonitis, etc.

3. **P. moniliformis.**—Found in Asia.

B. ORDER ACARINA

The Order Acarina includes the mites and ticks, and represents a type of degenerated arachnids that, from their parasitic existence or from other conditions of life, have become considerably modified. Thus, with the union of cephalothorax and abdomen the last traces of segmentation of the body are lost. They have six pairs of appendages—two pairs of mouth parts modified into a sucking organ and *four pairs of legs, which distinguish them from the parasitic hexapods or insects.* The larva as it escapes from the egg has three pairs of legs, and resembles certain imperfectly segmented parasitic insects, such as the lice.

The Acarina are cosmopolitan in their distribution, and have long been known to be human parasites. Recently it has been demonstrated that they also act as carriers of important disease, producing microörganisms which they transmit to man.

Life History.—The life history varies in different species, but in general it is as follows: The female lays eggs, from each of which a six-legged larva is hatched. This molts once or several times, and is gradually transformed into an eight-legged nymph which is active, usually feeds on a host, grows, molts again, and becomes an adult. The males are usually smaller and more active than the females. As a rule, both sexes take their nourishment from the host, which may be either a plant or an animal.

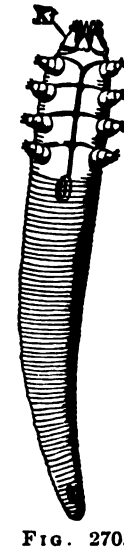


FIG. 270.—Demodex folliculorum, enlarged. *Kt.* biting jaws. (*After R. Blanchard in Brumpt.*)

Pathogenesis.—The Acarina are disseminators of diseases to man and animals. In man they spread relapsing fever, tick fever of the Rocky Mountains, etc. In animals they spread babesiases and spirochetiases. In plants they produce galls, etc. They are also the cause of skin diseases, such as scabies in man.

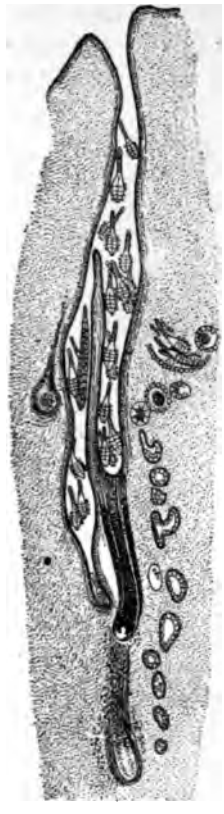


FIG. 271.—Demodex folliculorum in the hair follicle of a dog. (*After Neumann in Brumpt.*)

Classification.—The Acarina are divided into five groups: I. *Demodicoidea;* II. *Sarcoptoidea;* III. *Ixodoidea;* IV. *Gamasoidea;* V. *Trombididoidea.* Of these, only the first three are of importance in human parasitology.

I. DEMODICOIDEA

These are vermiform insects and occur as parasites of man and of the lower animals. The family includes only one genus, *Demodex.*

Demodex folliculorum (Simon, 1842).—This parasite (Fig. 270) is cosmopolitan and lives in the sebaceous follicles of the face of man. Other species are found in dogs, pigs, cattle, etc. The *male* measures 300 by 40μ and the *female* 380 by 45μ. Beyond a local irritation, the parasite does not produce any special symptoms in man. It is possible that it may act as a carrier of *Bacillus leprœ.*

II. SARCOPTOIDEA

This family comprises several parasitic species of the lower animals, and the genus *Sarcoptes*, one species of which—*S. scabiei*—is parasitic on man.

Sarcoptes scabiei, var. hominis (Linnæus, 1758).—The body is round or slightly oval, and set with bristles. Two anterior and two posterior pairs of legs are present, the latter being concealed beneath the body. The *female* measures 330 to 450μ by 250 to 350μ. It is oviparous. The *male* measures 200 to 235μ by 145 to 190μ.

Life History.—The female burrows into the skin and lays its eggs beneath the epidermis. On the sixth day the eggs hatch a six-legged larva, which, after several molts, on the sixteenth day becomes an eight-legged nymph. It molts again several times, and about the sixth week becomes an adult.

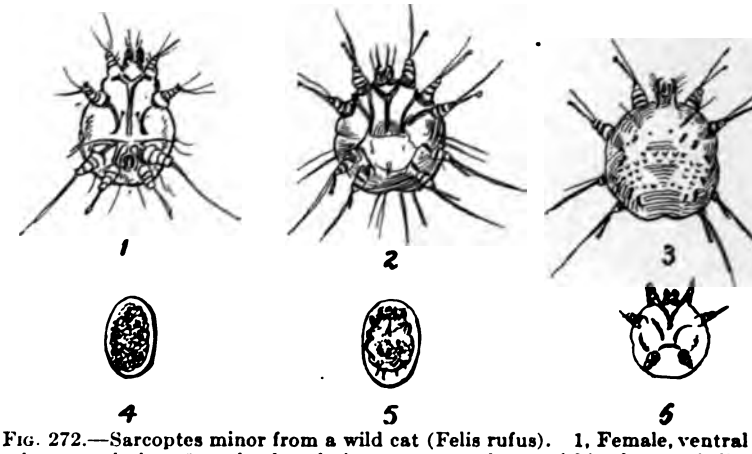


FIG. 272.—Sarcoptes minor from a wild cat (Felis rufus). 1, Female, ventral view; 2, male, ventral view; 3, male, dorsal view; 4, egg; 5, larva within the egg shell; 6, free six-legged larva.

Pathogenesis.—This parasite is the cause of scabies, or, as it is commonly termed, "the itch," in man, a condition characterized by a more or less severe dermatitis. The pruritus is most intense at night, when the patient retires. The lesions are more common at the sides of the fingers, and between them, on the backs of the hands, at the elbows, and not infrequently on the face. They appear as small streaks under the epidermis, brownish or blackish in color, because of the deposition of the eggs or the collection of dirt. Among cleanly persons these streaks are inconspicuous or invisible. The excoriation produced by scratching of the skin predisposes to bacterial infection, eczema, lymphangitis, etc.

Diagnosis.—The pleomorphism of the lesions, their localization, the nocturnal pruritus, and the presence of other cases in the same

family or in the same house, enable the diagnosis of the disease to be made without difficulty. With the aid of a magnifying glass it is easy to observe the color and extent of the grooves, which are about 2 to 4 mm. in length. The parasite and eggs may be seen under the microscope in fresh cover-glass preparations made from scrapings of this groove, suspended in a little water.

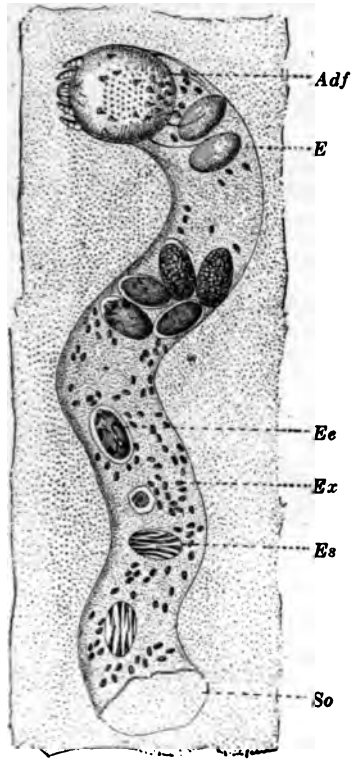


FIG. 273.

Treatment.—This consists in washing the part with warm water and soap for about thirty minutes, to be followed by alcohol and the application of sulphurated ointment. If possible, the patient should first take a bath and change his clothes.

Other parasitic species of domestic animals that occasionally are found in man are:

Sarcoptes scabiei var. equi, in horses; *S. scabiei var. ovis*, in sheep;



FIG. 274.

FIG. 273.—Sarcoptes scabiei. Diagram of a subcutaneous furrow. *Adf*, adult female; *E*, eggs; *Ee*, embryo egg; *Ex*, excrement; *Es*, egg shell; *So*, skin orifice. (*After Railliet in Brumpt.*)

FIG. 274.—Margaropus annulatus say, var. australis. Dorsal view of the male. (*After Castellani and Chalmers.*)

S. scabiei var. caprœ, in goats; *S. scabiei var. suis*, in pigs; *S. scabiei var. canis*, in dogs.

III. IXODOIDEA—THE TICKS

The tick family is of importance in human parasitology not only because some species are true parasites on man and animals, but because they act as intermediate hosts and transmitters of disease.

Morphology.—The tick is divisible into two parts: *head* and *body*. The rostrum or *capitulum* is the anterior structure of the head, con-

taining the mouth parts, and, in addition, a *neck* may be seen at the junction of the rostrum with the remainder of the body (Fig. 274).

The Head (Fig. 275), together with the mouth parts, is made up of three divisions: (1) A *base*, usually quadrangular in shape; (2) a *neck* behind the base, at the junction of the head with the body, and (3) a *haustellum* (rostellum), in front of the base, which is easily seen from above in the *Ixodidæ*, and consists of *hypostome*, *mandibles*, *palpi* on each side, and a sheath.

The hypostome (Fig. 275) is an elongated structure, consisting of two symmetrical halves, which contain numerous teeth or denticles on the ventral surface.

The mandibles, or cheliceræ (Fig. 275), are two in number, and are situated on each side of the median line and dorsal to the hypostome. They contain hook-like teeth and are directed backward.

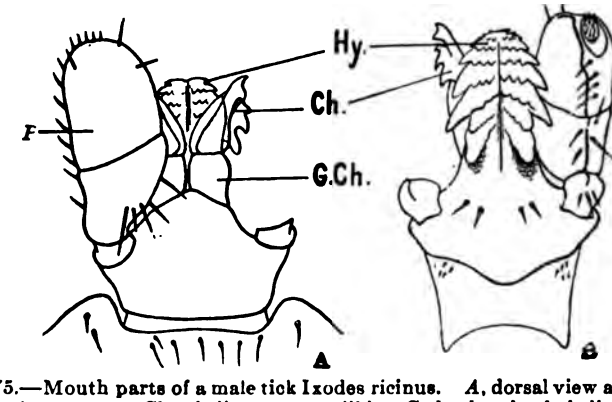


FIG. 275.—Mouth parts of a male tick Ixodes ricinus. *A*, dorsal view and *B*, ventral view. *Hy* hypostoma; *Ch*, chelicer or mandibles; *G.ch*, sheath of chelicer; *p*, palpes. × 70. (*After Nuttall and Warburton in Brumpt.*)

The mandibular sheath lies dorsal to the mandibles.

The palpi (Fig. 275), on each side of the base, are short, and are made up of four segments (apical, penultimate, antepenultimate, and basal).

The Body.—The body is divided into dorsal and ventral surfaces and anterior, posterior, and lateral margins.

The Dorsal Surface.—On the dorsal surface (Fig. 276) the following structures may be seen: (1) The *scutum*, in the center and anteriorly. This is somewhat triangular in shape and well marked in the *Ixodidæ*, and consists of a hard, chitinous plate with two longitudinal grooves; it is absent in the *Argasidæ;* (2) the *eyes*, situated at the margins of the scutum, are often absent; (3) the *dorsosubmedian porous plate*, which is a small, hard, chitinous plate on each side of the median line, and between the third and fourth legs; (4) the *posteromarginal festoons*,

when present, appear as eleven areas separated by grooves on the posterior margin between the stigmata; (5) the *dorsal grooves*, often absent; (6) the *dorsal plates;* (7) pits, hairs, and spines.

The ventral surface (Fig. 276) shows: (1) The *genital pore* in the median line, between the anterior and middle thirds of the body; (2) the *anus*, in the median line, behind, the posterior pairs of legs; (3) the *ventral shields* or *sclerites* in the male; (4) the *stigmata* on each side of the body, between the third and fourth pairs of legs in *Argasidæ*, and behind the fourth in the *Ixodidæ;* (5) genital and anal grooves, pits, pores, and hairs, when present.

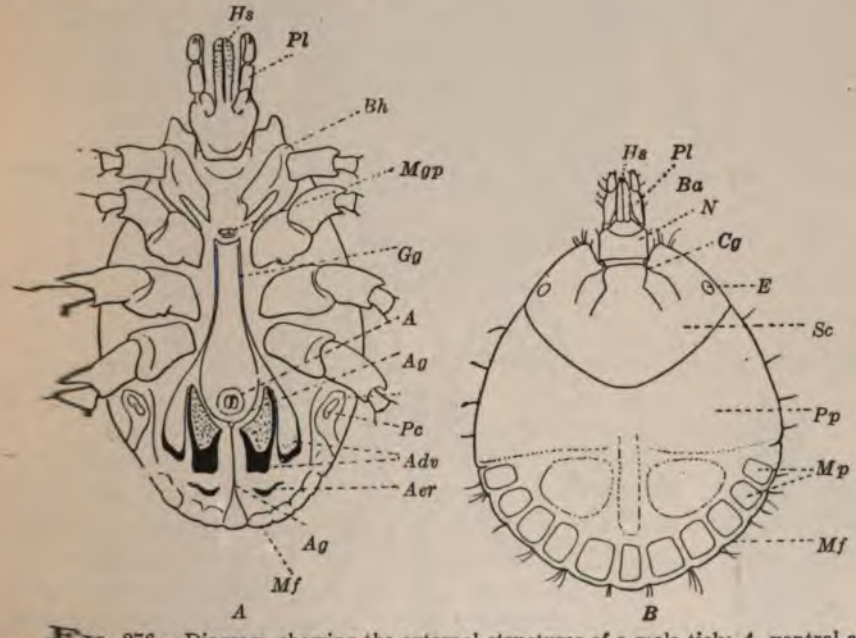


FIG. 276.—Diagram showing the external structures of a male tick: *A*, ventral aspect of Hyalomma ægytium: *B*, dorsal aspect of Amblyomma hirtum. *Hs*, hypostome; *Pl*, palpes; *Bh*, bifid hip; *Mgp*, male genital pore; *Gg*, genital groove; *A*, anus; *Ag*, anal groove; *Pc*, peristigmatic comma shape plate or sclerite; *Adr*, adanal ridges; *Acr*, accessory ridge; *Mf*, marginal festoons; *B*, base; *N*, neck; *Cg*, cervical groove; *E*, eyes; *Se*, scutum; *Pp*, posterior part; *Mp*, marginal plate. (*After Neumann in Brumpt.*)

The Legs.—These consist of six segments: *coxa*, *trochanter*, *femur*, *patella*, *tibia*, and *tarsus*, the last, in *Ixodidæ*, being provided with a *pulvillus* (Fig. 277).

The Glands.—In some species a large *cephalic gland* is present opening dorsally at the junction of the rostrum with the body. Two large racemose *salivary glands* open into the cavity of the mouth, and there are also numerous *dermal glands.*

The Intestinal Tract.—The digestive system (Fig. 278) consists of a mouth, pharynx, esophagus, middle gut, a large food reservoir or

stomach, a central canal or intestine, a rectum, into which th[illegible] ghian tubules open, and an anus.



FIG. 277.—Leg of an ixodes (Margaropus) showing the ambulacres. (*After Salm and Stiles in Brumpt.*)

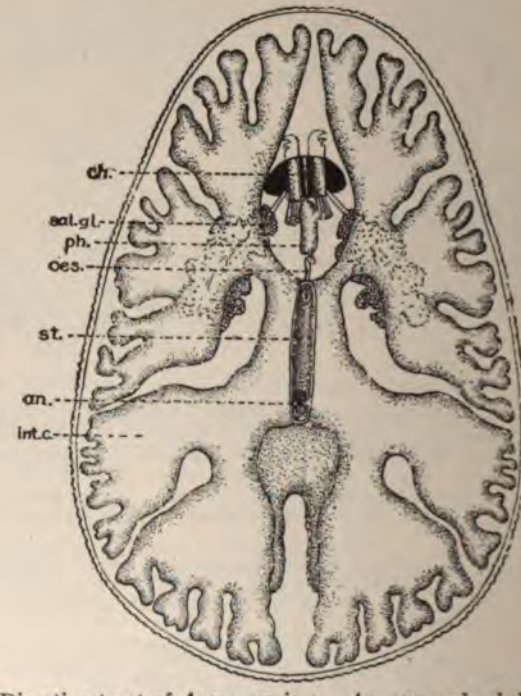


FIG. 278.—Digestive tract of *Argas persicus*. *An*, anus; *ch*, chelicera; *int.c*, intestinal ceca; *es*, esophagus; *ph*, pharynx; *sal.gl*, salivary glands; *st*, stomach. About 20. (*From Robinson and Davidson in Chandler.*)

Respiratory System.—This consists of a system of trache[illegible] opens into the stigmata or spiracles at each side of the body.

Circulatory System.—As in insects, this system consists of a dorsal heart and distributing vessels.



FIG. 279.—Copulation of the male, *M* and female, *F* tick. (*After Sambon, Castellani and Chalmers.*)

Excretory System.—This consists of Malpighian tubules that open into the rectum.

Reproductive System.—The *male* generative organs consist of tubular testes, one or two vasa deferentia, glands, ejaculatory duct, and penis. The genital pore is situated ventrally, at about the level of the second pair of legs. The *female* reproductive organs consist of simple ovaries, oviduct, spermatheca, and genital opening, the last being situated ventrally at about the junction of the third and middle third of the body.



FIG. 280.—Texas fever tick, *Margaropus annulatus*, laying eggs. (*After Graybill in Chandler.*)

Life History.—The male and female live on the host. The male, which is the smaller, may not uncommonly be seen attached to the ventral surface of the female (Fig. 279). Under normal conditions, after fertilization has taken place and the female has become engorged with blood, she falls to the ground and lays eggs (Fig. 280). A six-legged larva is eventually hatched from the egg and attaches itself to a host, sucks its blood, drops off, molts, and becomes an eight-legged nymph. The nymph again attaches itself to a host, sucks blood, and again drops off, molts, and attains adult growth (Fig. 281).

The larva has six legs, a complete alimentary tract, but no stigmata or reproductive organs. The nymph has eight legs, a complete alimentary tract, stigmata, and the rudiments of sexual organs.

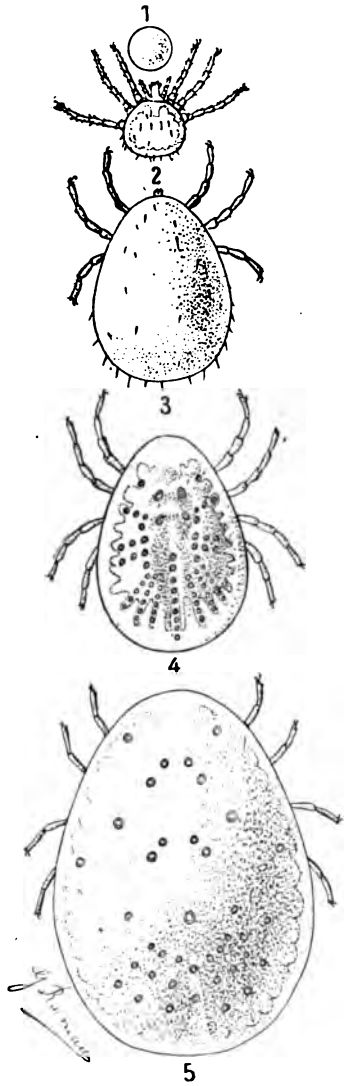


FIG. 281.—Diagram of the evolution of *Argas persicus*. 1, Egg; 2, hexapods larva (after 8 days); 3, the same enlarged; 4, octopods nymphs (after 10 days); 5, adult tick. (*After Brumpt.*)

In some species the larva attaches itself to the host and becomes a nymph and adult without dropping to the ground. The time occupied in complete evolution varies from two to four months, according to the species. In *Margaropus decoloratus* the time consumed in evolution is as follows: Oviposition after falling to the ground, one to four weeks; incubation, three to eight weeks. The larva may remain dormant for months; first molt occurs in three days to one week; it becomes a nymph in about one week—an adult, in one to two months; copulation takes place in two to three weeks, after which it gorges itself with blood and drops to the ground (Lounsbury).

The life history of a tick shows, therefore, that the progeny, and not the adult, as is the case with mosquitos, transmit the virus, this being due to the fact that, once attached to the host, the adult tick holds on until it becomes engorged with blood, when it drops to the ground for the purpose of oviposition, and subsequently dies. The virus is introduced into the body of the tick with the blood, undergoes evolution, infests the ovaries and eggs, and passes to the larvæ, which in turn transmit it to another host while sucking the blood of the latter. In this connection, however, it may be mentioned that in some species the female does not die after oviposition occurs, and may attack another host. It may also happen—and perhaps this is more common than is generally believed—that the tick may become detached by mechanical agencies or following death of the host, and again attack another host, in this way serving as a direct transmitter of the virus.

Habitat.—The ticks are terrestrial animals, and are found preferably in sunny, sandy localities, or where there is low-growing vegetation. They are rarely parasites of any special host, but attack animals of different species.

Pathogenesis.—Generally speaking, the ticks are merely *accidental parasitis* of man. Their greatest interest centers about the part they play as agents in the transmission of such microörganismal diseases of man as relapsing fever, Rocky Mountain fever, and probably of certain blood parasites, and a number of diseases of the lower animals. The following is a list of the known species of ticks that transmit diseases to man and the lower animals:

Ornithodoros moubata, the carrier of *Spirocheta duttoni,* the cause of relapsing fever in man; *Argas persicus, Spirocheta appendiculatus,* and *Rhipicephalus simus,* carriers of *Babesia bigemina,* the cause of babesiasis in cattle; *R. everti,* which transmits *B. equi; R. sanguineus,* which transmits *B. canis;* and *R. bursa,* transmitting *B. bovis; Margaropus annulatus, Babesia annulatum,* and *Hemophysalis leachi,* transmitting *B. canis.*

Classification.—Following the classification adopted by Castellani and Chalmers, the ticks are divided into two families: Family I, *Ixodidæ,* or true ticks, and Family II, *Argasidæ.*

Family I. *Ixodidæ.*—The members of this family are characterized by the presence of a *scutum.* The *rostrum* or *capitulum* (mouth part) is long and prominent, and is easily seen from the dorsal surface as an elongated, beak-like proboscis. A *pulvillus* is attached to the tarsus in the adult, and the second pair of legs is the shortest and the fourth pair the longest. *Stigmata* are situated posterior to the coxa of the fourth leg. The male is smaller and stouter than the female. The family comprises several genera: (1) *Ixodes;* (2) *Amblyomma;* (3) *Rhipicephalus;* (4) *Margaropus;* (5) *Dermacentor,* and (6) *Hemophysalis,* etc. Each genus has several species.

1. *Genus Ixodes.*—Eyes absent; palpi long and hollowed on the internal surface; preanal groove open posteriorly; tarsi have no terminal spurs; stigmata comma-shaped.

2. *Genus Amblyomma.*—Eyes present; rostrum long; palpi valvate; anal groove semicircular, open anteriorly; stigmata triangular.

3. *Genus Rhipicephalus.*—Capitulum hexagonal; male with anal plates; stigma comma-shaped; eyes present.

4. *Genus Margaropus.*—Capitulum hexagonal; male with anal plates; stigma round; eyes present.

5. *Genus Dermacentor.*—Capitulum rectangular; male without anal plates; stigma comma-shaped; eyes present.

6. *Genus Hemaphysalis.*—Capitulum rectangular; male without anal plates; stigma comma-shaped or circular; eyes absent.

FAMILY II. ARGASIDÆ.—This family is differentiated from the *Ixodidæ* by the absence of a scutum; by the fact that the mouth parts are short and not prominent from above; by the absence of a pulvillus in the adult; by the presence of stigmata between the coxa of the third and fourth legs; and by the nocturnal habit. They do not remain on the host, and resemble bugs more than ticks. The family comprises four genera, of which three need be considered here: (1) *Argas;* (2) *Ornithodoros;* (3) *Alectorobius.*

1. *Genus Argas.*—Body flat and oval in shape; eyes absent.

2. *Genus Ornithodoros.*—Thicker body; tips of the palpi visible from above; eyes often present; presence of preanal, post-anal, and supra-coxal grooves; presence of folds of the skin from *sclerites* on each side of palpi.

3. *Genus Alectorobius.*—The same as *Ornithodoros* except for the absence of *sclerites* on each side of the palpi.

The two families comprise numerous species, and their number is still increasing as new varieties are being discovered, but only relatively few are of interest in human parasitology.

FAMILY IXODIDÆ

1. **Ixodes ricinus** (Linnæus, 1758).—This is sometimes called the castor-oil tick (Fig. 282) from the resemblance the female bears to a castor-oil bean. The *male* measures 2.5 by 1.5 mm. The scutum is a deep red-brown; the genital pore is situated at the level of the third coxa; pregenital and anal shields are present, and the capitulum is long. When young, the body of the *female* is flat and oval, and when adult and engorged, it resembles a castor-oil bean. It measures 10 to 11 by 6 to 7 mm., and is of an ashy color. The genital pore is situated at the level of the fourth coxa. Stigma is whitish in color.

Habitat and Life History.—This tick is cosmopolitan in habit and attacks man and almost any terrestrial animal. The female drops from the host and lays her eggs on the ground. The larva hatches in from four to six weeks, and attaches itself to the host for about one week, after which it drops and becomes a nymph in about four weeks. It now attaches itself to a second host, drops, and then to a third host, becoming an adult in about eight weeks.

Pathogenesis.—The adult tick may become infected with *Babesia bigemina* as the result of sucking the blood of infected cattle, and the larva and nymph of the new generation may transmit the parasite to fresh cattle.

2. **Amblyomma hebreum** (Koch, 1844).—This tick is common in Africa. It attacks man and animals. The *male* has a white scutum and green marginal festoons. The *female* when fully replete measures 24

by 15 mm., and has a whitish brown or white scutum. The life history is similar to that of *Ixodes ricinus*.

Pathogenesis.—It transmits the virus of a disease known as "*heart water*" that attacks sheep and goats. In man its bite is said to give rise to a morbid condition known as "tick-bite fever," which is accompanied by headache, adenitis, and other symptoms, and which, according to Nuttall, may be mistaken for *bubonic plague* or pest.

3. **Dermacentor venustus** (Banks).—This species (Fig. 283) is very common in North America. When empty, the body is narrower anteriorly, but when replete with food, the female is nearly globular in shape and somewhat constricted at the level of the stigmata. The male measures 5 by 2.5 mm. When empty the female body is about

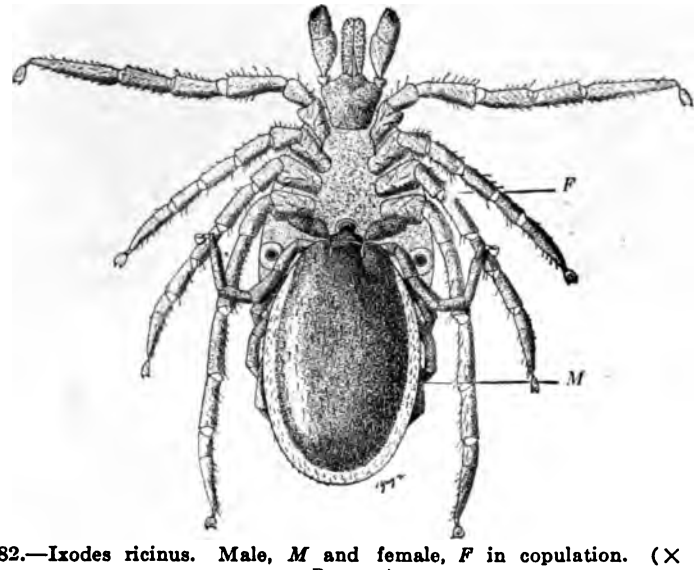


FIG. 282.—Ixodes ricinus. Male, *M* and female, *F* in copulation. (× 12 *after Brumpt.*)

the same size as the male, but when replete with food it measures 16 by 10 mm.

Pathogenesis.—It is the transmitter of the virus of Rocky Mountain fever.

4. **Rhipicephalus sanguineus** (Latreille, 1806).—This species is cosmopolitan, and is found in many domestic animals, but is rarely seen in man. It transmits *Babesia canis*.

5. **R. bursa** (Canestrini and Fanzago, 1878).—Transmits *B. ovis* to sheep.

6. **R. simus** (L. Koch, 1844).—Common in Africa. It attacks several domestic animals. It transmits *Theileria parva* to cattle. It

is also responsible for the transmission of "tick-bite fever" (Sant' Anna, Nuttall).

7. **Margaropus annulatus** (Say, 1821).—Common in the southern United States, Africa, and South America. It transmits *Babesia bigemina*, the cause of Texas or red-water fever in cattle (Fig. 280).

8. **Hemaphysalis leachi** (Audouin, 1827).—This species is the common day tick of South Africa. The male measures 3 by 1.5 mm., and the female 9 by 5 mm. It transmits *Babesia canis*.



FIG. 283.—Spotted fever tick. *Dermacentor venustus*, male ♂ and female ♀. (*After Chandler.*)

FAMILY ARGASIDÆ

1. **Argas persicus** (Oken, 1818).—This tick (Fig. 284) is cosmopolitan, being found in Asia, Africa, and America. The body is oval and brownish-red in color. The *male* measures 4 to 5 by 3 mm.; the *female*, 7 to 10 by 5 to 6 mm.

Pathogenesis.—According to Balfour, this tick transmits *Spirocheta marchouxi* in fowls.

2. **Ornithodoros moubata** (Murray, 1877).—The body of this tick (Fig. 285) is oval and wider behind than in front. Eyes are absent. The color varies from yellow to brown, according to the age. The cuticle is covered with numerous small, hemispheric prominences; the dorsal surface is marked with three or four pairs of pits, and the ventral shows a preanal sulcus, a supracoxal groove, and two or three pairs of post-anal longitudinal grooves, which are best seen in the female. The male measures about 6 mm. in length and the female from 12 to 14 mm.

Pathogenesis.—It is the transmitter of *Spirocheta duttoni*, the

cause of African relapsing fever in man, and according to Wellman and Feldman, possibly also of *Filaria perstans*. In the body of the adult tick the spirochete passes to the eggs in an evolutional form of

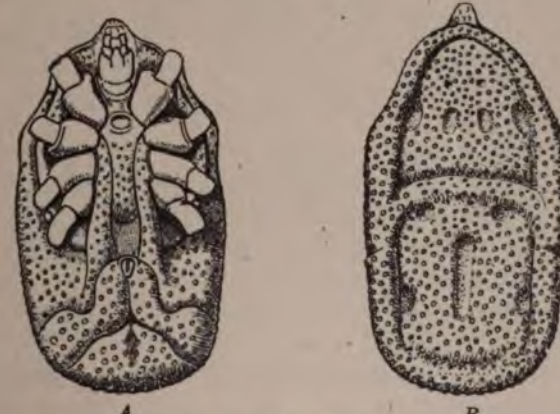


FIG. 284.—Persian tick or fowl tick, *Argas persicus*. × 5. (*After Braun in Chandler.*)



FIG. 285.—The tampan, *Ornithodorus moubata*. × 3. (*After Chandler.*)

small granules, and as such are transmitted by the larva and nymph to man, in the body of which they develop into spirochetes (Leishmann). The virus may be transmitted to the third generation of the tick (Moellers).



A *B*

FIG. 286.—Ornithodoros turicata. *A*, ventral and *B*, dorsal view. (× 14 *After Nuttall and Warburton in Brumpt.*)

3. **Ornithodoros savignyi** (Audouin, 1827).—This tick is common in Africa and India and perhaps elsewhere. The body is oval, and yellow or brown in color, according to the age. It has two pairs of eyes above the base of the first and between those of the second and third pairs of legs. It attacks man and animals.

Pathogenesis.—According to Brumpt, this tick, like *O. moubata*, transmits *Spirocheta duttoni*, the cause of African relapsing fever in man.

4. **Ornithodoros turicata** (Duges, 1876).—This tick is common in Mexico and Central America. The anterior part of the body is much narrowed. Eyes are absent.

Pathogenesis.—According to R. Blanchard, this tick possibly transmits the relapsing fever of Colombia.

5. **Alectorobius talaje** (Guerin-Meneville, 1849).—This tick is common in Mexico, Central America, and South America, where it is regarded as a great pest and is commonly known as *chinche* (a name also given to the bed bug). It is nocturnal in habit, lives in the houses in the crevices of the walls, furniture, beds, etc., and bites man during sleep. The bite is painful and is not uncommonly followed by suppuration. The body of the tick is somewhat oval in shape, pointed anteriorly, and measures 5 to 6 mm. in length.

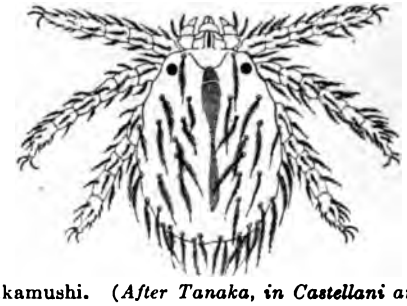


FIG. 287.—Akamushi. (*After Tanaka, in Castellani and Chalmers.*)

FAMILY TROMBIDIDÆ

1. **Akamushi or Kedani.**—This larval mite belongs to the family, *Trombididæ*, which causes "tsutsugamushi," or Japanese river fever. It is orange-red in color, and measures 0.16 to 0.38 mm. in length by 100 to 240μ in breadth. The life history is not well known.

2. **Leptus autumnalis** (Shaw, 1790).—This larva is the harvest-mite or harvest-bug of the south of England, Germany, and France, which attacks dogs, cats, and man.

Other species are: *L. americanus* and *L. irritans*, "red bug," found in the United States and Mexico. They cause itching, redness, swelling, and even suppuration. The life history is not known, and only the larva appears to be a parasite.

FAMILY TARSONEMIDÆ

Pediculoides ventricosus (Newport, 1850).—This mite lives in the straw and stalks of cereals. The adult breaks directly from the egg, and its bite will cause itching, painful eruption, and fever.

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CHAPTER XXII

CLASS INSECTA

GENERAL CONSIDERATION OF INSECTS

Morphology and Structure.—Life History and Development.—Classification.

The insects, as has previously been stated, are arthropods whose body is divided into three distinct parts: head, thorax, and abdomen.

Insects are of great importance in human parasitology, since the recent work of Manson, Ross, Grassi, Klein, Chagas, Castellani, and others has demonstrated that they transmit the parasites of malarial fever, filariasis, trypanosomiasis, etc. It has also been shown that they serve as carriers of a number of bacterial diseases.

Morphology and Structure.—Besides the head, thorax, and abdomen, insects possess specialized appendages in the form of wings, mouth parts, etc., which constitute a distinctive feature of this group.

The Head.—The skull is usually proportionate to the size and power of the mouth parts. It is divided into the following parts: (1) The *epicranium*, which occupies the greater part of the dorsal surface; (2) the *front*, in the middle of the face; (3) the *vertex*, above the front, forming the summit of the head; (4) the *clypeus*, situated in front, between the *front* and the upper lip or *labrum;* (5) the *gena* and *post gena*, or cheeks at the sides; (6) the *gula*, on the under side, bearing the under lip or *labium;* (7) the *occiput*, that part nearest to the prothorax and surrounding the opening known as the *occipital foramen*, through which the esophagus, nerves, and other structures pass into the thorax; (8) the *tentorium*, that internal part anterior to the *occipital foramen;* it affords muscular attachment and holds the cephalic ganglia and esophagus in place.

The Thorax.—The thorax, or middle region, is that portion behind the head and in front of the abdomen. It is divided into three segments: *prothorax* in front; *mesothorax* in the middle, and *metathorax* behind. Each of the three segments bears a pair of legs. The dorsal surface of the thoracic segments is called the *notum* or *tergum;* the ventral *sternum* and the sides are known as the *pleurom*. In addition, the pleurom is divided into two *sclerites* (pleurites), separated by an oblique suture, the anterior part of which, coming in contact with the sternum, is termed the *episternum;* the other, the *epimeron*. These terms as applied to particular segments of the thorax are indicated

by the prefixes *pro-*, *meso-*, and *meta-;* thus *prosternum*, *pro-episternum*, etc.

The Abdomen.—The abdomen or hindmost region typically consists of ten segments. In a few instances (orthoptera) more may be present, whereas in others the number is apparently or actually less on account of the presence of modifications of the first segment in relation to the thorax or of the last segments for sexual purposes. A typical abdominal segment (alike as the thorax) bears a dorsal plate or *tergum* and a ventral plate or *sternum*, the two being connected by a pair of *pleural membranes* that facilitate the respiratory movements of the tergum and sternum. Most of the abdominal segments, the first

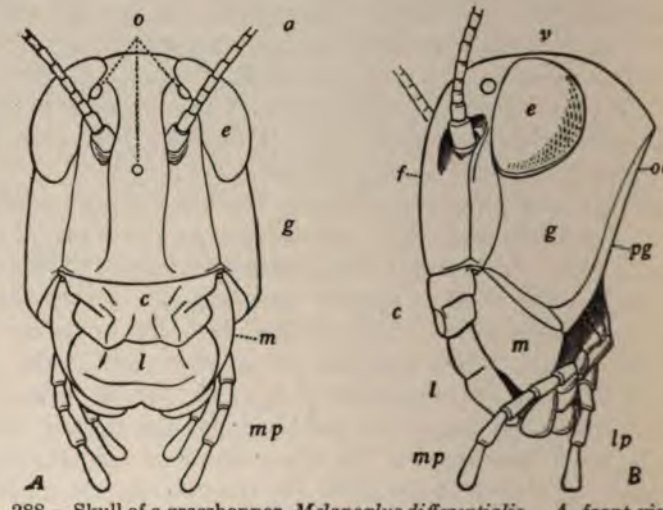


FIG. 288.—Skull of a grasshopper, *Melanoplus differentialis*. *A*, front view; *B*, side view. *a*, Antenna; *c*, clypeus; *e*, compound eye; *f*, front; *g*, gena; *l*, labrum; *lp*, labial palpus; *m*, mandible; *mp*, maxillary palpus; *o*, ocelli; *oc*, occiput; *pg*, post-gena; *v*, vertex. (*After Folsom.*)

seven or eight, have *spiracles*, one on each side, situated near the pleural membrane.

The Appendages.—The different varieties of specialized appendages in insects may properly be described as—(1) Biting or sucking; (2) locomotor; (3) pleopoda; (4) wings.

1. *Biting or Sucking Appendages.*—The mouth parts of insects (Figs. 288, 290, 291) present a great range of variations, but most of the orders fall into two groups: *mandibulate*, or biting, and *suctorial*, or sucking types. The mandibulate group probably represents the primitive type from which the suctorial has been derived.

Mandibulate Type.—This (Fig. 290) type consists of the following parts: (1) The *labrum*, or upper lip, which is a single plate hinged to the clypeus; it has the property of moving up and down and to some extent

also of protrusion and retraction. It covers the mandible in front and draws the food back to that organ. (2) Under the labrum and clypeus, in the roof of the pharynx, is the *epipharynx*, which is made up of teeth, tubercles, or bristles, and serves to hold food or as an organ of taste (Packard). (3) The *mandibles*, or jaws proper, which are two in number, move in a transverse plane. They are situated on the side

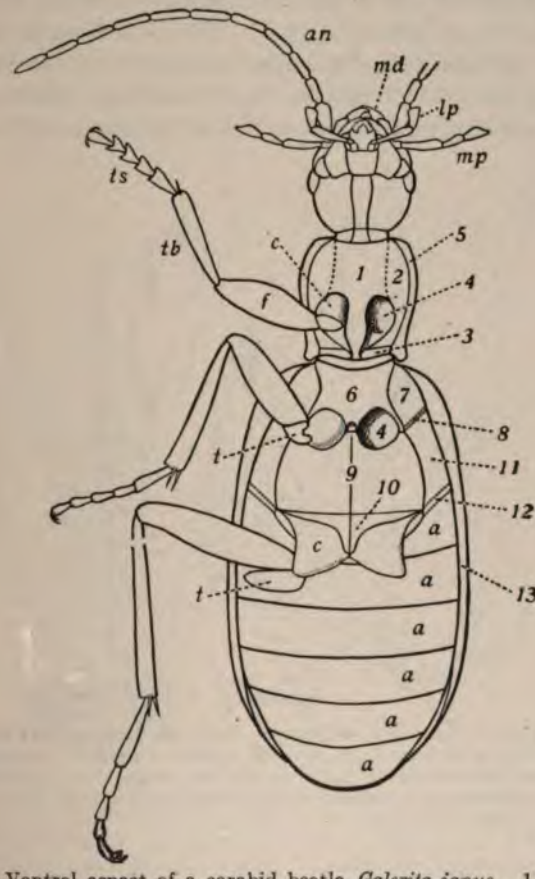


FIG. 289.—Ventral aspect of a carabid beetle, *Galerita janus*. 1, prosternum; 2, propisternum; 3, propimeron; 4, coxal cavity; 5, inflexed side of pronotum; 6, mesosternum; 7, mesopisternum; 8, mesopimeron; 9, metasternum; 10, antecoxal piece; 11, metapisternum; 12, metapimeron; 13, inflexed side of elytron; *a*, sternum of an abdominal segment; *an*, antenna; *c*, coxa; *f*, femur; *lp*, labial palpus; *md*, mandible; *mp*, maxillary palpus: *t*, trochanter; *tb*, tibia; *ts*, tarsus. (*After Folsom.*)

posterior to the labrum. (4) The *maxillæ*, or underjaws, also two in number, are more complex than the mandibles, and consist of several sclerites (*palpus*, *galea*, and *lacinia*) hinged to the skull by means of a *cardo*. (5) The *labium*, or under lip, may properly be compared to a pair of united maxillæ. It forms the floor of the pharynx, and assists

in carrying the food to the mandibles and maxillæ. (6) The *hypopharynx*, or tongue, is a fleshy organ, and is usually joined to the base of the labium. In insects the salivary glands generally open at the base of the hypopharynx.

Suctorial Type.—In the suctorial or houstellate type of insects, the mouth parts, owing to their great variation and complexity, are not well understood, but in general they are said to correspond to those parts in the mandibulate type. The mouth parts of the female mosquito, for instance (Fig. 291), are arranged in the form of a long and slender proboscis, which shows the following modifications: The labrum and epipharynx combine to aid in forming a sucking tube; the

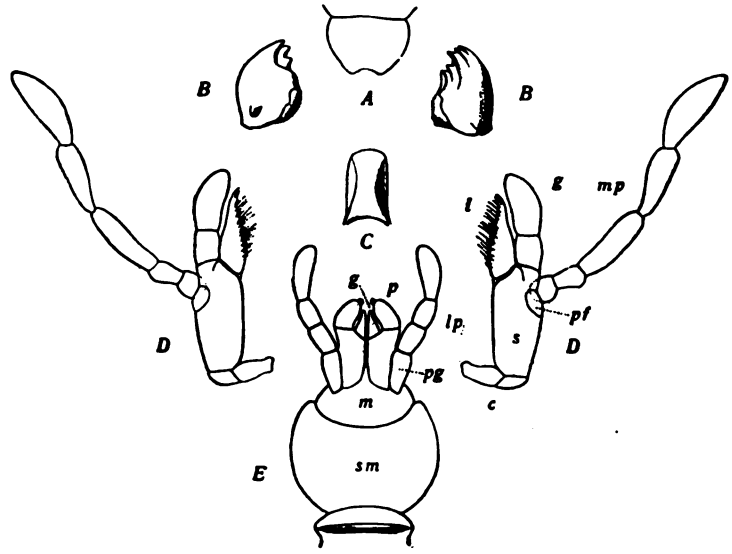


FIG. 290.—Mouth parts of a cockroach, *Ischnoptera pennsylvanica*. *A*, labrum; *B*, mandible; *C*, hypopharynx; *D*, maxilla; *E*, labium; *C*, cardo; *g* (of maxilla), galea; *g* (of labium), glossa; *l*, lacinia; *lp*, labial palpus; *m*, mentum; *mp*, maxillary palpus; *p*, paraglossa; *pf*, palpifer; *pg*, palpiger; *s*, stipes; *sm*, submentum. *B*, *D* and *E* are in ventral aspect. (*After Folsom.*)

mandible and maxillæ are slender, linear, piercing organs; the maxillæ, in addition, are distinctly barbed, and especially well adapted for cutting, acting like a saw, whereas the mandibles are finely pointed for piercing. The hypopharynx is also slender and linear, and serves to conduct the saliva, which acts as a lubricant. The labium is modified into a sheath that incloses the other mouth parts when these are not in use. In addition, the extreme tip of the labium is modified into two lobe-like structures termed *labella*, which probably act as sensory organs. The esophagus is dilated to form a bulb or sucking organ, from which muscles pass to the skeletal parts. When these muscles con-

tract, the bulb dilates, and, acting as a pump, sucks in fluids (blood or water) which are forced back into the stomach by contraction or by the elasticity of the bulb itself, regurgitation being prevented by a valve.

The male mosquito does not suck blood, and the mouth parts differ from those of the female in that the mandibles are aborted, the maxillæ are rudimentary, the hypopharynx coalesces with the labium, and the œsophagus has no bulb.

In the tsetse fly, *Glossina morsitans*, the proboscis is about as long as the head. The mouth parts, which serve for biting and sucking, consist of four parts: the *labium*, *labrum*, *epipharynx*, and *hypopharynx*.

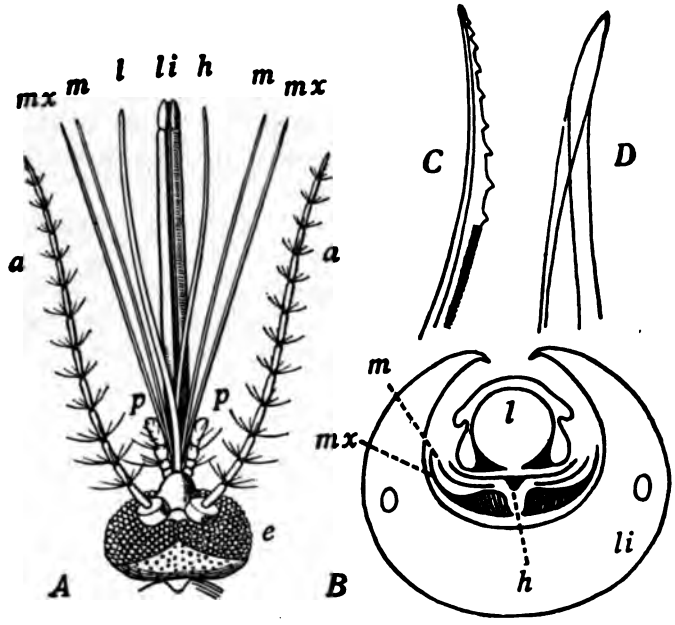


FIG. 291.—Mouth parts of female mosquito, *Culex pipiens*. *A*, dorsal aspect; *B*, transverse section; *C*, extremity of maxilla; *D*, extremity of labrum-epipharynx; *a*, antenna; *e*, compound eye; *h*, hypopharynx; *l*, labrum-epipharynx; *li*, labium; *m*, mandible; *mx*, maxilla; *p*, maxillary palpus—*B*. (*After Dimmock in Folsom.*)

The labium forms a sheath for the labrum, epipharynx, and hypopharynx, which are modified into piercing organs or barbed stylets that are especially well adapted for penetrating deep into the skin.

The mouth parts of the stable-fly, *Stomoxys calcitrans*, as in *Glossina*, are also modified into biting and sucking organs.

The mouth parts of the house-fly, *Musca domestica*, are modified into a trumpet-like proboscis that is adapted for sucking and licking, but not for biting or piercing, whereas among the *Hemiptera* the mouth parts of bedbugs are modified into piercing organs.

2. *Locomotor Appendages.*—The locomotor appendages or legs in almost all full-grown insects and in most larvæ are six in number, and correspond to one pair for each segment of the thorax. In the Acarina, however, an additional cephalic pair of legs usually occurs, due to the fusion of the thorax with the head. The leg is made up of five segments: *coxa, trochanter, femur, tibia,* and *tarsus.* The tarsus, which is rarely single-jointed, is made up, as a rule, of five segments, the last of which bears a pair of claws. In addition, in some insects there is a pad called the *pulvillus* or *empodium.* In flies this shows glandular hairs and enables the insect to walk on smooth surfaces or upside down.



FIG. 292.—Leg of a beetle, *Calosoma calidum.* *c*, coxa; *cl*, claws; *f*, femur; *s*, spur; t^1–t^5, tarsal segments; *tb*, tibia; *tr*, trochanter. (*After Folsom.*)

3. *Pleopoda Appendages.*—These are pseudo-feet or rudimentary legs. They are small and inconspicuous, commonly situated on the abdomen (*prolegs*), and vary in function. They may serve as gills or as supports for the gills, as points for the attachment of eggs, as organs for the transfer of sperms, or for purposes of running or creeping.

4. *The Wings.*—The grouping of insects into a separate class is based largely upon the fact of whether or not they possess wings. The latter, in conjunction with the character of the mouth parts, have furnished the most reliable basis for purposes of classification. Typically, there are two pairs of wings, one anterior and the other posterior, attached to the mesothorax and metathorax respectively. The prothorax bears no wings, and when, as in diptera, only one pair of wings is present, these are usually the anterior. In bird-lice, fleas, and most parasitic insects the wings have degenerated.

Morphology and Venation of Wings.—The shape of wings varies considerably, but as a rule they are triangular and present three margins: (1) Front or *costal;* (2) outer or *apical,* and (3) inner or posterior, *anal.* They are divided by longitudinal veins or nervures which, according to location, are termed *costal, apical,* and *anal veins* respectively, the anal veins being further subdivided into *cubital, medial,* and *radial,* and the costal into *costa* and *subcosta.* All veins are numbered, according to their location, as *first, second,* etc. (Figs. 293, 294).

The spaces between the veins are called *cells,* and these are numbered the same as the veins; thus the space between the first and the second medial vein is called the *first medial cell,* and that between the second and third, the *second medial cell,* etc.

This distribution of the veins is of great importance in classification, since these structures show so wide a range of variations that by its means an expert may often refer a detached wing to its proper genus or even to its species.

Not uncommonly the wings may show hairs or certain markings or spots that may serve as a reliable means of differentiation, as is the case with *Anopheles*, which have spotted wings, and *Culex*, which is devoid of spots, etc.

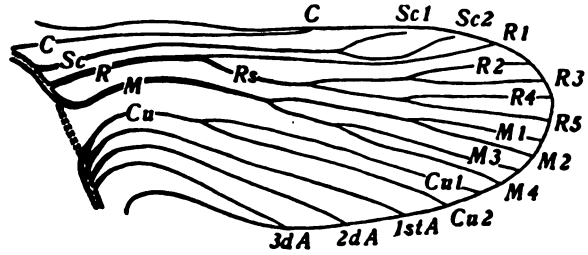


FIG. 293.—Hypothetical type of venation. *A*, anal vein; *C*, costa; *Cu*, cubitus; *M*, media; *R*, radius; *Sc*, subcosta. (*After Comstock and Needham, in Folsom.*)

From what has been said it may be seen that these appendages in insects occupy a constant position in the body; thus, the antennæ are in the head and mouth parts; the maxillipedes, legs, and wings are on the thorax; the pleopods and pseudo-feet, when they exist, are on the abdomen. Somites bearing antennæ or jaws belong to the head; those bearing legs or wings belong to the thorax. The cephalothorax is that region of the body that bears legs as well as antennæ and jaws.

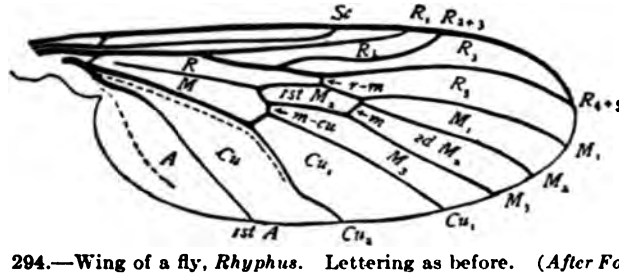


FIG. 294.—Wing of a fly, *Rhyphus*. Lettering as before. (*After Folsom.*)

The Cuticle.—The cuticle or skin of arthropods (Fig. 295) differs from that of worms in that it is permeated with a leathery substance known as *chitin*, which is the basis of the skeletons of all arthropods. Chitin is but slightly or not at all affected by acids and alkalis, but is soluble in potassium hypochlorid and in boiling sulphuric acid.

The chitinous integument or external skelton is a secretion of the hypodermic cells. It consists of three layers: (1) the cuticle; (2) the

subcuticle, and (3) the hypodermic cells. The hypodermic cells contain pigment, fat-drops, etc., and are limited outwardly by the integument and inwardly by a delicate hyaline *basement membrane*.

Cuticular Appendages.—Externally the cuticle may be smooth, wrinkled, striated, granular, tuberculated, or molded into a variety of shapes, some of which are adaptive, whereas others apparently are merely ornamental. These appendages occur in the form of hairs, spines, and scales.

Hairs and spines are always present, and may be simple, toothed, or branched. The hairs arise from modified hypodermic cells, and may be tactile, protective, olfactory (moth), or auditory (male mosquito) in function. The glandular hairs found in the pulvilli of many flies, beetles, etc., enable these insects to walk on slippery surfaces. The twisted or branched hairs of bees serve to gather and hold the pollen grains.



FIG. 295.—Section through integument of a beetle, *Chryosbothris*. *b*, basement membrane; c^1, primary cuticula; c^2, secondary cuticula; *h*, hypodermis cell; *n*, nucleus. (*After Tower in Folsom.*)

Scales are present in all Lepidoptera and in some other insects (Coleoptera, Diptera, etc.). Although variable in shape, most scales are usually flat and bear markings that are characteristic of the species. That hairs and scales serve as equivalents is shown by—(1) the complete transition from hairs to scales that may be found on the same insect; and (2) the fact that both arise from enlarged or modified hypodermic cells (Fig. 314).

Glands.—Glands of various forms and functions are found in certain insects; *e.g.* (1) *glandular hairs* and spines, found in the feet of flies; (2) *repellent glands*, which secrete various offensive fluids; thus the blood of the Spanish fly contains cantharidin, a caustic substance. Many Carabidæ eject from a pair of anal glands a pungent and often corrosive fluid. The salivary glands of piercing flies secrete an irritant substance: that of the mosquito secretes an anticoagulant, and the poison gland of wasps secretes a poisonous substance. Conversely certain insects have glands that secrete an odorous substance that serves to attract insects of the opposite sex. (3) *Wax glands* are present especially in Hymenoptera and Hemiptera. In the worker honey-bee the wax exudes from hypodermic glands that appear on the under side of the abdomen as four pairs of wax scales. (4) *Silk glands*, although most characteristic of Lepidoptera, occur also in the cocoon-spinning larvæ of several other insects and in larvæ whose pupæ are suspended from a silken support. The silk glands of caterpillars and

silkworms (Lepidoptera) are homologous with the salivary glands of other insects. They usually open through the hypopharynx, which is modified to form the spinning organ or *spinneret.* The glands have their origin in an invagination of the pharynx (ectodermal), and in the silkworm, where the gland is about five times longer than the body, it consists of a glandular convoluted portion—silk reservoir—a pair of common ducts, a thread press, and a spinneret. (5) *Salivary glands.* In the house-fly these glands consist of two long, tubular structures on each side of the head and neck. They unite to form a common duct that opens through the hypopharynx. In mosquitos (*Culex* and *Anopheles*) each gland consists of three lobes—two large ones with one small one between (poison gland), on each side. They open into a duct that unites with its fellow of the opposite side to form a common duct, emptying near the hypopharynx.



FIG. 296.—Diagram to indicate the course of the blood in the nymph of a dragon fly, *Epitheca.* *a*, Aorta; *h*, heart; the arrow shows directions taken by currents of blood. (*After Kolbe in Folsom.*)

The Muscular System.—Insects have a surprisingly large number of muscles. It has been estimated that a caterpillar, for example, has about 2000 muscles. The muscular power of insects is marvelous. According to Plateau, the weakest insects can pull five times their own weight, and the average insect about twenty times its weight which is in marked contrast to man, who can pull about 0.86 times his weight, and the horse, that pulls but from 0.5 to 0.83. This may be accounted for by the fact that the specific gravity of chitin is lower than that of bones, and, furthermore, the external skeleton in insects affords a muscular attachment of the strongest kind.

The most important muscles in most insects are: (1) The muscles of the legs and wings, when these are present, for locomotion; (2) the *longitudinal sternals* and the *longitudinal tergals,* which serve to telescope the abdominal segments; (3) the *oblique sternals,* which bend the abdomen; (4) the *tergosternal* or vertical expiratory muscles, which draw the tergum and sternum together, and (5) the muscle of the mouth parts, which serves for biting or sucking, as the case may be.

Circulatory System.—The circulatory system in insects (Fig. 296), unlike that of vertebrates, does not consist of a system of closed blood-

vessels. The *hemolymph* wanders freely through the body cavity, and finally enters the pulsating dorsal vessel. This dorsal vessel is a deli



FIG. 297.—Blood corpuscles of a grasshopper, *Stenobothrus*. *a–f*, Corpuscles covered with fat-globules; *g*, corpuscle after treatment with glycerine, showing nucleus. (*After Graber in Folsom.*)

cate tube that extends dorsally along the abdomen and thorax in the median line, and is divided into an abdominal portion or *heart*, consisting of several pulsating chambers and a thoracic portion or *aorta*. The tube is usually closed posteriorly, but is provided laterally on each side, and between the chambers, with a valvular opening or *ostium* that permits the ingress of blood, but prevents its egress. The tube is open anteriorly.

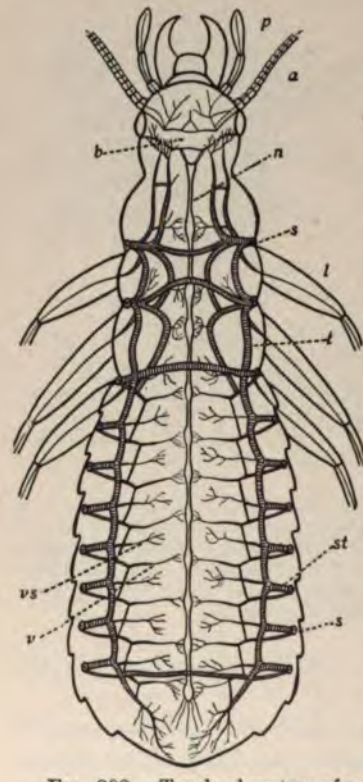


FIG. 298.—Tracheal system of an insect. *a*, Antenna; *b*, brain; *l*, leg; *n*, nerve cord; *p*, palpus; *s*, spiracle; *st*, spiracular or stigmatal, branch; *t*, main tracheal trunk; *v*, ventral branch; *vs*, visceral branch. (*After Kolbe in Folsom.*)

Circulation.—The hemolymph, flowing through the spaces between the muscles, trachea, nerves, etc., and bathing all the tissues, enters the chambers in the dorsal vessel through the *ostia*, passes through the aorta, escapes into the tissue, and reënters the dorsal chambers.

The Hemolymph.—This is a watery fluid or *plasma*, varying in color, and containing *leukocytes*, but no erythrocytes. The leukocytes are ameboid, and from 6 to 30μ in diameter. They often appear yellowish or red in color, owing to the presence of drops of fat on the surface of the cell (Fig. 297). The hemolymph is not concerned with the aëration of the tissue, that function being relegated to the tracheal system, its principal function probably being that of aiding nutrition.

Respiratory System.—Respiration in insects is accomplished by means of an elaborate system of branching tubes, known as the *tracheæ*, through which the air is conveyed to the remotest tissues of the body. The

air enters the tracheæ through small openings, called *spiracles*, which are arranged segmentally at the sides of the body. Each spiracle is provided with a short tube that opens into a *main* tracheal trunk extending along each side of the body. This trunk divides and subdivides into numerous branches, which eventually become extremely minute, and are capable of penetrating between the muscle-fibers; the ommatidia of the compound eye possibly is also penetrated by these capillaries. In many cases each main longitudinal trunk gives off three large branches in each segment: (1) A *dorsal* branch for the dorsal muscle; (2) a *visceral*, for the alimentary tract and reproductive system; and (3) a *ventral*, for the ventral muscle and ganglia.

Reproductive System.—In insects the sexes are divided, hermaphroditism occurring only as an abnormality. Reproduction by budding never takes place, but parthenogenesis and pedogenesis are met with in some groups. Parthenogenesis, in some instances, bears a definite relation to the life history; thus in Aphides (plant-lice) many successive broods of females alone may be generated, these bringing forth living young, but in autumn, males also appear, and fertilized eggs are laid that last during the winter. In bees parthenogenesis determines the sexes, since males are produced only from unfertilized eggs. Pedogenesis occurs in *Miastor*, a Cecidomyid fly. The larva gives rise to new larvæ inside of its body, and these escape by rupture of the mother larva. After several successive generations of this kind the resulting larvæ pupate and produce normal male and female flies.

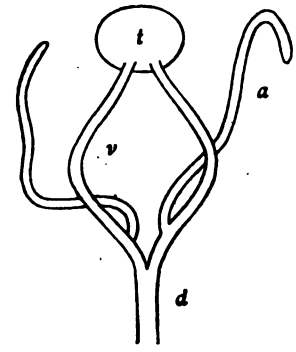


FIG. 299.—Reproductive system of male Lepidoptera. *a*, Accessory gland; *d*, ejaculatory duct; *t*, united testes; *v*, vas deferens. (*After Kolbe in Folsom.*)

The male reproductive organs consist of a pair of *testes*, usually in the form of a group of tubes or sacs, but may be single. These open into *vasa deferentia*, which unite to form a common *ejaculatory duct* and end in a *penis*. The *vas deferens* is at times dilated into a *seminal vesicle*. Not uncommonly one or more pairs of accessory glands open into the vas deferens or ejaculatory duct.

The female reproductive organs (Fig. 300) consist of a pair of *ovaries*, composed of one or more tubes, and a pair of *oviducts* that unite to form a common duct, the *vagina*, which opens on the exterior, often through an *ovipositor*.

Life History and Development.—One of the most characteristic phenomena in the life of arthropods in general, and of insects in particular, is the change of form that takes place after they leave the egg. This is termed *metamorphosis*. Thus, from the egg of a house-

fly a *larva* is hatched; this grows and becomes a *pupa*, which in turn develops into an *imago*. The larva of Diptera is sometimes called a "maggot;" the larva and the pupa of the butterfly, are called respectively "caterpillar" and "chrysalis." This metamorphosis is not, however, always complete, and may sometimes be absent; hence the subdivision of insects into—(1) *Holometabola*, those undergoing complete metamorphosis (Lepidoptera, Diptera, Hymenoptera, etc.); (2) *Heterometabola:* In these the pupa stage is usually absent, and the imago is essentially similar to the young at birth, except that it has wings and is sexually mature (Orthoptera, Hemiptera, Odonata, etc.). Here the metamorphosis is *direct* or incomplete. In heterometabolous insects there is no distinction between larva and pupa, and the name *nymph* is commonly applied to that stage of growth between the egg and the imago. (3) *Ametabola*, those in which there is no metamorphosis (Thysanura and Collembola). In these the form at hatching is retained essentially throughout life, wings are absent, and there is no change of habit. Insects, may be divided, therefore, into *Metabola*, which comprise the Holometabola and Heterometabola, and *Ametabola* (Packer).

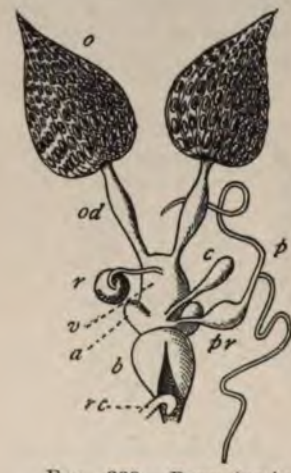


FIG. 300.—Reproductive system of queen honey bee. *a*, accessory sac of vagina; *b*, bulb of stinging apparatus; *c*, colleterial, or cement, gland; *o*, ovary; *od*, oviduct; *p*, poison glands; *pr*, poison reservoir; *r*, receptaculum seminis; *rc*, rectum; *v*, vagina. (*After Leuckart in Folsom.*)

Molting Stadium and Instar.—During growth the skin of an insect is shed at certain intervals. This process is called *molting* or *ecdysis*. With each molt the appearance of the insect is more or less altered. The intervals between molting is known as *stadia* or *stages*. The term *instar* has been suggested to designate any particular stage in the development; thus the insect at hatching is called the *first instar;* after the first molting, *second instar*, etc.

The Egg.—The egg of an insect, as of all animals, is a single cell with a large *nucleus* (germinal vesicle), a *nucleolus*, *yolk* (deuteroplasm), and *vitelline membrane*, arising from the ovarian cells, all inclosed in a shell or chorion. The eggs are exceedingly variable in form, but as a rule, they are globular, oval, or elongated. The surface may be smooth, molded, or mosaic-like, and frequently covered with ridges. The chorion is always the seat of one or more openings, the *micropyle*, for the entrance of the spermatozoa. The eggs are also variable in size, some being scarcely visible to the naked eye, whereas others are several millimeters in length. As a rule, when the eggs are laid, the

process is accompanied by the ejection of a fluid secreted by the seminal gland, which, leading into the vagina, serves as a means of attaching the egg to surrounding objects (house-flies), or holding or cementing them together (*Culex*).

The Larva.—Brauer, Packard, and others recognize two types of the larvæ of insects: (1) *Thysanuriform* and (2) *eruciform* larvæ. The term *thysanuriform larva* is applied to many larvæ because of their resemblance to *Thysanura*. This represents a primitive type in evolution, and is common to insects that undergo incomplete or no metamorphosis (*heterometabolous* and *ametabolous*), of which the bedbug is an example. The larva is usually flat, provided with antennæ, mouth parts, and well-developed, long legs. It is sometimes termed a *nymph*. The *eruciform larva* is derived from the *thysanuriform* type, and is common to insects subject to complete metamorphosis (holometabolous), of which the caterpillar and maggot are examples. In these the body is cylindric and often fleshy, and the legs, antennæ, and mouth parts are diminished in size on account of partial or complete disuse. Extreme reduction is seen in the maggot of parasitic flies and of other Diptera that secure their food with little or no exertion. In these the cuticle is thin, the legs are absent, and the head is rudimentary or absent.

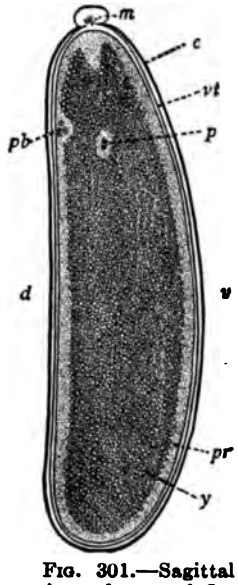


FIG. 301.—Sagittal section of egg of fly, *Musca*, in process of fertilization. *c*, chorion; *d*, dorsal; *m*, micropyle, with gelatinous exudation; *p*, male and female pronuclei, before union; *pb*, polar bodies; *pr*, peripheral protoplasm; *vs*, ventral; *vt*, vitelline membrane; *y*, yolk. (*After Henking and Blochmann in Folsom.*)

As the eruciform type is derived from the thysanuriform, types intermediate between the two naturally exist and are represented by "transitional forms."

Growth.—The larval stage is manifested chiefly by very remarkable growth. Thus, according to Trouvelot, a certain caterpillar (*Telea polyphemus*) attains 4.140 times its original weight in fifty-six days, and a maggot 200 times its original weight during the course of its larval existence.

Ecdysis.—The process of *ecdysis*, or molting, is usually as follows: The old cuticle becomes dried, shrinks, becomes detached from the body, splits near the head, and is pushed backward by contractions of the larva. The number of molts varies; thus the house-fly has four, some caterpillars have five, and the ticks have one, three, or more. The appearance of the larva is usually changed after each molting.

The Larvæ.—The larvæ (Figs. 302, 303) exhibit a large variety of adaptations in conformity to environments, and those that are

most active during this stage, as, for instance, the tick, have well-developed sense organs, good powers of locomotion, etc. The chief function of the larva is to feed, and consequently it is subject to modifications dependent upon the food environment. On the other hand,

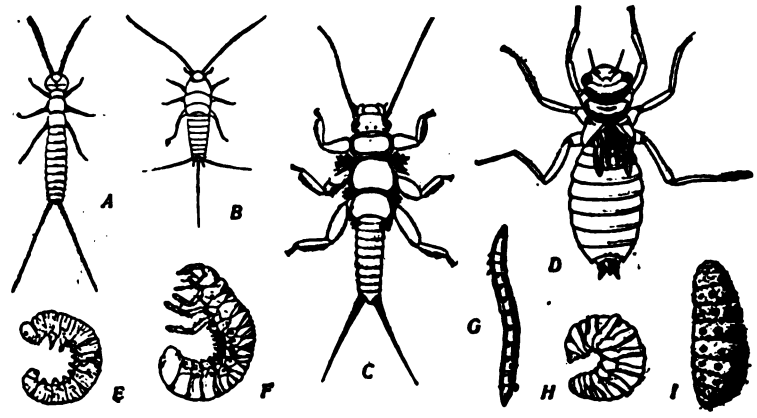


FIG. 302.—Types of larvæ. *A*, *B*, thysanura; *C*, *D*, thysanuriform nymphs; *E–I*, eruciform larvæ. *A*, *Campodea*; *C*, *Lepisma*; *C*, perlid nymph (Plecoptera); *D*, *Libellula* (Odonata); *E*, *Tenthredopsis* (Hymenoptera); *F*, *Lachnosterna* (Coloptera); *G*, *Melanotus* (Coleoptera); *H*, *Bombus* (Hymenoptera); *I*, *Hypoderma* (Diptera). (*After Folsom.*)

the fleshy maggot, embedded in an abundance of food, is almost headless and devoid of legs.

The Pupa.—The pupa stage is common only to holometabolous insects, such as Lepidoptera and Diptera. During this stage the insect

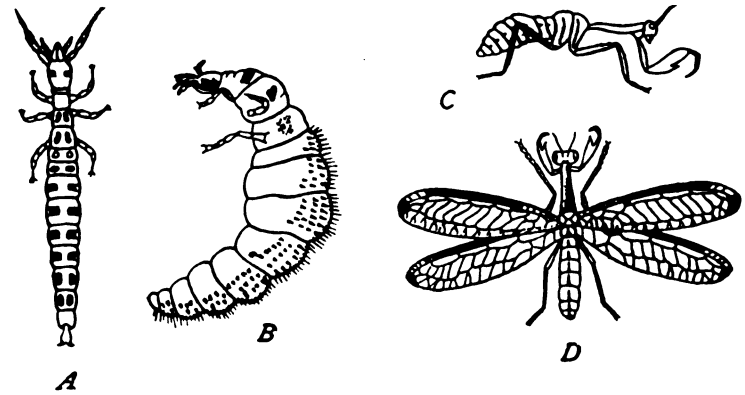


FIG. 303.—*Mantispa*. *A*, larva at hatching—*thysanuriform*; *B*, same larva just before first moult—now being *eruciform*. *C*, imago, the wings omitted; *D*, winged imago slightly enlarged—*A* and *B* after *Brauer*; *B* and *D* after *Emerton*, *Packard's Book of Entomology*, in *Folsom*.

may be active or inactive, but takes no food, is covered by a protective envelop, and may remain in this state over the winter. The pupa in the mosquito is active.

During the quiescent period of reconstruction, profound changes take place. Among the holometabolous insects the function of nutrition is relegated to the larval stage, and that of reproduction to the imaginal stage, and as both stages are so dissimilar in adaptation to the environment, a gradual change from one to the other makes a temporary cessation of external activities necessary. Thus, during the pupa stage the biting mouth parts of a caterpillar are gradually changed into the sucking organs of the butterfly; the rudimentary mouth parts of a maggot are changed into the specialized biting or sucking organs of the fly, etc. In addition, during this stage reproductive organs, wings, and other structures adapted to the new environment are developed.

Classification.—The number, shape, arrangement, and structure of the mouth parts; the presence or absence of wings, and their number and structure; the occurrence of a complete or an incomplete metamorphosis—all these permit the division of insects into several orders, viz.: (1) Hemiptera; (2) Diptera; (3) Siphonaptera; (4) Lepidoptera; (5) Hymenoptera; (6) Neuroptera; (7) Pseudoneuroptera; (8) Orthoptera; (9) Coleoptera, etc. Of these, only the Hemiptera, Diptera, and Siphonaptera contain the parasitic insects of man, a description of which, together with their characteristics and classification, is given in the following chapters.

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CHAPTER XXIII

CLASS INSECTA (Continued)

ORDER I. HEMIPTERA

This order, described by Linnæus in 1742, comprises the vast number of insects known collectively as *bugs*. The *mouth parts* are usually suctorial, the whole rostrum being adapted both for piercing and for sucking. Wings may be absent (Siphunculata—aptera) or present (Heteroptera, Homoptera). In the largest groups of Hemiptera (Heteroptera) the wings are thick and leathery at the base, and thin and membranous at the apex; they lie flat on the back, and are divided into three parts: *corium*, *clavus*, and *membrane*. Metamorphosis is incomplete, except in the male *Coccidiæ* and related forms. The order is divided into three suborders: (1) Anoplura; (2) Heteroptera; and (3) Homoptera, of which only the first two contain species parasitic to man.

SUBORDER ANOPLURA

This group is characterized by the absence of wings; the mouth parts are not jointed, forming a *rostrum* or proboscis that is armed with hooklets. The eyes are without facets, and there are a pair of from three to five-jointed antennæ. The legs have hook-like terminal joints that are adapted for clinging. The last abdominal segment is notched in the female and rounded in the male. Metamorphosis is incomplete. The order embraces the family *Pediculidæ*.

Family Pediculidæ

These are anoplura whose head is narrower than the thorax. The family contains the lice that are found all over the world, infesting man and the lower animals. Their bites cause marked irritation of the skin, which may become infected and give rise to impetigo. The insects are said to transmit blood parasites (*trypanosomes* and *hemogregarins*) and typhus fever. The family comprises six genera, of which only two, *Pediculus* and *Phthirius*, need be described here.

Genus 1. *Pediculus.*—The members of this genus are characterized by having an abdomen made up of 7 or 8 segments, without lateral tubercles; the second segment has one pair of spiracles.

1. Pediculus capitis (De Geer, 1778).—This is the common head louse. It is gray in color. The abdomen is made up of seven seg-

ments. The *male* measures 1.6 by 0.7 mm. with rounded posterior end. The *female* measures 2.7 by 1 mm., and the posterior end of the abdomen is notched.

Habitat and Life History.—This louse inhabits the scalp and is found in the hair; rarely it may invade the beard. The female lays



FIG. 304.—Pediculus capitis, ♀, female; ♂, male.

from 50 to 60 eggs, which are firmly attached to the hair by the secretion of the cement gland. In about six days these eggs hatch into a larva that develops into an adult in from two to three weeks.

Pathogenesis.—The bite of this louse is a source of irritation that varies greatly in different individuals. When the irritation is marked and the epidermis is abraded by scratching, infection and impetigo may follow. This louse has been said to transmit some of the blood parasites and possibly the virus of typhus fever.

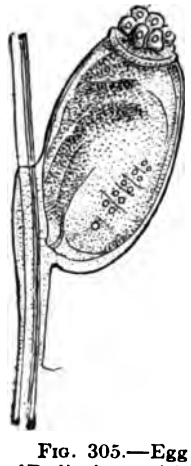


FIG. 305.—Egg of Pediculus capitis attached to a hair, enlarged. (*After Brumpt.*)

Treatment.—This consists of proper cleaning of the head and the application of paraffin oil or equal parts of petroleum and olive oil. White or red precipitate mercurial ointment is also effective.

2. **Pediculus corporis** (De Geer, 1778).—This louse is believed by some to be identical with *P. capitis;* it is, however, larger, and the abdomen contains eight segments and six stigmata (Fig. 306). The *male* measures 3 by 1 mm. and the *female* 3.3 by 1.1 mm.

Habitat.—The insect lives in the clothes and is found on the surface of the body only at the time of biting.

Life History.—This is the same as that of *P. capitis*, except that the eggs are attached to the clothes instead of to the hairs.

Pathogenesis.—The bite causes irritation and itching and predisposes to bacterial infection. This insect has been said to transmit the parasite of relapsing fever (Mackie) and of typhus fever (Nicolle, Compte, Conseil).

Treatment.—Disinfection of the clothes.

Genus 2. *Phthirius.*—The abdomen is six-segmented, with lateral tubercles; the second segment is provided with three pairs of spiracles.

Phthirius pubis (Linnæus, 1758).—This is the pubic or "crab louse," commonly found in the hair of the pubic region. It occurs more frequently in men than in women. The body is generally flat and broad, the head is round, and the neck distinct. The abdomen contains six segments. The legs are provided with claws. The *male* measures 1 mm. and the *female* about 1.5 mm.

Pathogenesis.—The bite of this louse is the cause of much irritation and may set up a dermatitis accompanied by discoloration of the skin. This is known as *phthiriasis.*

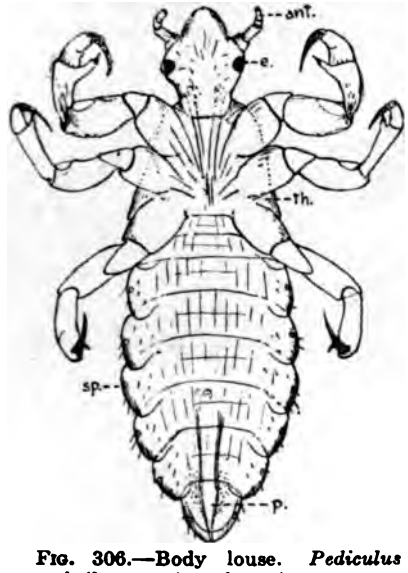


FIG. 306.—Body louse. *Pediculus corporis* (*humanus*), male. *Ant*, antenna; *e*, eye; *p*, penis; *sp*, spiracles; *th*, thorax. × 25. (*After Chandler.*)



FIG. 307.—Adult female, ♀ and egg, ov, of Phthirius pubis attached to hair.

Treatment.—White or red precipitate mercurial ointment, or equal parts of petroleum and olive oil applied locally.

SUBORDER HETEROPTERA

The members of this suborder are characterized by the presence of two different pairs of wings—hence the name. The front pair is membranous or horny, or semi-membranous and semi-horny; the posterior pair is wholly membranous. In some parasitic species both pairs of wings may be absent.

The anterior wings are called *hemelytra*, and usually consist of three portions: the *clavus*, or basal portion, next to the scutellum; the *corium*, or middle portion, and the *membrane*, or outer portion.

These insects, as a rule, eject a pungent and repulsive secretion

from glands that open on each side ventrally, at about the middle of the metasternum and at the level of the third pair of legs. The suborder is divided into several families, of which only the *Cimicidæ* and *Reduviidæ* contain species that are parasitic to man.

Family 1. Cimicidæ

Body flat; ocelli absent; hemelytra short, so that the abdomen is left uncovered; tarsi have three joints. The family contains four genera, but only the genus *Cimex* need be considered here.

***Genus Cimex*.—Head short and broad, with two prominent eyes; four-jointed antennæ; hemelytra rudimentary; prothorax semilunar; abdomen uncovered and containing seven segments and an anal appendage; legs slender; proboscis fixed into a groove under the head and prothorax.**



Fig. 308.—Cimex lectularius.

1. Cimex lectularius (Linnæus, 1758).—This insect, commonly known as the bedbug, chinche in some Latin American countries, is found in all parts of the world. The Romans called it *cimex*, and it is said to have been introduced into England in 1502. Both males and females feed on blood, and they are said to be disseminators of relapsing fever and of other protozoa and bacterial diseases.

The body of the insect is reddish-brown in color The proboscis consists of an upper part, the *labrum*, and a lower portion, the *labium*, within which are four stylets: two outer (the mandibles) and two inner (the maxillæ). The *prothorax* is semilunar in shape. The *mesothorax* is triangular, with the apex directed posteriorly. The *metathorax* is covered dorsally by the hemelytra, which are two chitinous mesothoracic plates. Posteriorly, it is covered with hairs. It is from 4 to 6 mm. in length by 3 mm. in width, and the female is larger than the male. The male can be recognized by the presence of a spicule, which is easily visible on the ventral surface posteriorly.

The digestive tract is made up of a mouth, pharynx, esophagus, crop, middle gut or stomach, intestine, rectum, and anus. Beneath the pharynx is a syringe-like organ or salivary pump, into which the salivary glands open; these glands are situated on each side of the digestive tract. The Malpighian tubules are situated on each side of the intestine.

Habitat.—Bedbugs live in cracks in floors, walls, and furniture. They feed exclusively on blood, and usually bite at night, although they may also feed during the day. They usually attack man, but

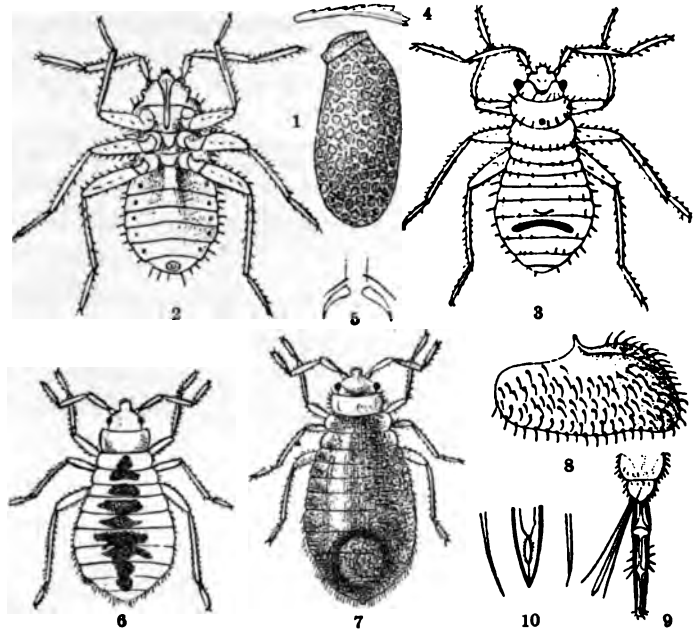


FIG. 309.—Cimex lectularius. 1, Egg; 2 and 3, ventral and dorsal view of the larva; 4, claws; 5, hair; 6, larva after moulting; 7, the same after feeding; 8, wing; 9, proboscis; 10, the same enlarged. (*After Marlat in Brumpt.*)

may bite and feed on lower animals. Not infrequently they migrate from house to house. Bedbugs, it is believed, may live for months or years without food, since they have been found alive in houses uninhabited for prolonged periods, but in this connection it should be remembered that they also feed on animals (rats, cats, birds, etc.). They are doubtless capable of resisting starvation for a considerable period of time. Placed under confinement during the summer months, the author was unable to keep them alive without food for longer than six weeks.

Life History.—The female lays about 50 eggs three or four times during the year, and complete development requires from seven to eleven weeks, according to the environment. The eggs, which are

oval in shape and white in color, measure 1.1 mm. in length and, under favorable conditions take about seven to ten days to hatch. The larva grows and molts about five times at intervals of eight days, after which the adult stage is reached, which is manifested by the appearance of the wing-pads.

Pathogenesis.—Cimex lectularius is believed to be the intermediate host of *Spirocheta recurrentis*, the cause of European relapsing fever in man. The insect has also been suspected of acting as a transmitter of several metazoan, protozoan, and bacterial parasites, and thereby causing such diseases, as *filariasis*, *malarial fever*, *trypanosomiasis*, *Oriental sore*, plague (Verjbitski), *tuberculosis*, *leprosy*, etc., a statement

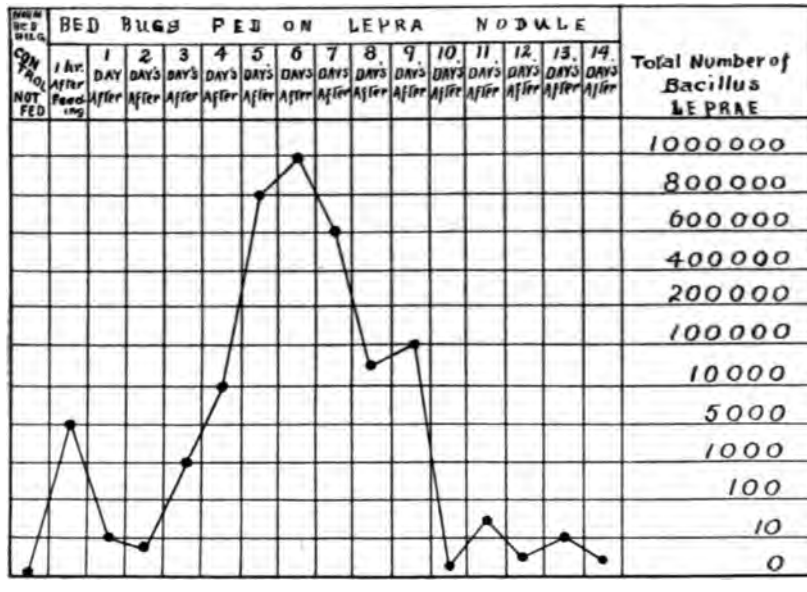


FIG. 310.—Chart illustrating the numerical behavior of Bacillus lepræ within the bedbug *Cimex lectularius* fed on lepra nodules.

that has not been satisfactorily proved. The author has observed living *microfilariæ* in the body of the insect eight days after feeding on the blood of a patient infested with *F. bancrofti*, but failed to recognize any development in the worm. He also believes that he has observed *Bacillus lepræ* multiply in the body of the bedbug, and then gradually, in about fifteen days, disappear, either by elimination with the feces or as the result of digestion.

Seven days after feeding on a lepra nodule of a patient, the author permitted four bedbugs to feed upon a healthy person, with negative results after ten years of observation. That the bedbugs contained lepra bacilli in their bodies at the time of the experiment was proved

by microscopic examination of the insects. In sections and on spreads made of the bedbugs, crushed in a little water after feeding Hansen's bacillus was found in abundance.

2. **Cimex rotundatus** (Signoret, 1852).—This is the Indian bedbug. It is common in Asia, but is also occasionally seen in America. It is differentiated from *C. lectularius* by being darker in color; in addition the head is shorter and narrower, the prothorax has rounded borders, and the abdomen is somewhat larger and narrower. It measures 4 to 5 mm. by 3 mm.

Habitat and Life History.—These are the same as in *C. lectularius.*

Pathogenesis.—This insect transmits *Leishmania donovani,* the parasite of kala-azar, or tropical splenomegaly (Patton), and *Trypanosoma cruzi,* the parasite of American trypanosomiasis (Brumpt).



FIG. 311.—Cimex rotundatus.

The pathogenesis of other bedbugs, such as *C. hirundinis* (Jenyns, 1839), *C. columbarius* (Jenyns, 1839), *C. ciliatus* (Eversman, 1841), etc., has not been determined.

Prophylaxis.—Bedbugs are especially common in tropical countries. The most important point in the prophylaxis is, of course, cleanliness. The use of painted iron bedsteads, which can easily be taken apart and cleaned, is to be recommended. Mattresses and pillows should be covered with canvas, which can be washed. Acetic acid, camphor, carbolic acid, and petroleum, applied once every one or two weeks, are effective insecticides. The eggs are very resistant to these applications, hence the necessity of applying the antiseptic at regular intervals so as to destroy the larva when it hatches. The room should be fumigated with formaldehyde or sulphur, two pounds being burned for every 1000 cubic feet of space. After fumigation the room should be kept closed for from four to six hours.

Family 2. Reduviidæ

Head long and narrow; cylindric or conic in shape; ocelli large, prominent, and situated posteriorly or absent. Proboscis short and curved; antennæ long and slender at the tip; legs long, and tarsus three jointed; elytra, when present, having three divisions; thorax slightly or not at all constricted: abdomen oval in shape, and having seven segments; wings well developed, and when at rest, overlapping, covering almost the entire back of the abdomen *Lamus* (*Conorhinus*) *megistus*. This family comprises many genera, for example, *Lamus* (*Conorhinus*), *Reduvius*, *Coriscus*, *Rasahus*, and *Melanolestes*. In addition to these an aquatic family, the *Hydrometridæ*, is of importance because, as shown by Patton, they may serve as hosts for the Crithidia, and other protozoa.



Fig. 312. Conorhinus megistus, the carrier of Trypanosoma cruzi. (*After Chagas.*)

1. **Lamus** (**Conorhinus**) **megistus** (Burmeister).—This species is common in the mining regions of Brazil, and is a carrier of *Trypanosoma cruzi*, which is the cause of trypanosomiasis Americana, Chagas disease, or "Oppilaçao." This insect attacks men and animals, and because of its habit of biting the face, is called "Barberio" by the natives. On being imbibed with the blood, the trypanosome undergoes multiplication and metamorphosis into Crithidia in the stomach and intestine of the insect. Typical trypanosomes are found in the rectum, and may be deposited with the excrement in the mucosa of the mouth, eyes, nose, etc., of man. Metrocyclic forms are also found in the salivary glands of the insect. Infection takes place by the active penetration of the mucous membrane by the trypanosomes or through the bite of *Lamus megistus*, infected with the parasite.

This insect is dark brown in color. The body is flat; the head is narrow and jointed; the antennæ are long and slender, and the thorax is provided with well-developed wings. When first laid, the eggs are white. The larvæ hatch in about twenty days, molt twice, and become pupæ, which also molt and develop into adults.

2. **L. sanguisuga** (Leconte, 1855).—This insect, known also as "blood-sucking cone nose," is found west of the Alleghenies. Its bite is painful, and is followed by swelling, nausea, etc.

3. **L. mexicanus** (Leiva, 1912) is found in Mexico.

4. **L. nigrovarius** is widely distributed in South America, where it is known variously as *Bichuque*, *Benchuca*, and *Vinchuga*. It is nocturnal in habit.

5. **L. rubrofasciatus.**—This species is commonly found in India.

6. **Rasahus biguttatus** (Say, 1831).—This variety is found most frequently in Cuba, Panama, and in certain regions of South America. It preys on bedbugs, but may also bite man.

7. **Melanoleste picipes** is the "kissing bug" of the United States.

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CHAPTER XXIV

CLASS INSECTA (Continued)

ORDER II. DIPTERA

The Diptera are insects provided with a well-developed pair of anterior wings and a rudimentary posterior pair in the form of *halteres*, or balancers; in parasitic species, however, the wings may be rudimentary or absent. The mouth parts are well developed and adapted for piercing, lapping, rasping, sucking, etc. They are subject to complete metamorphosis. The larvæ do not, as a rule, have true legs. The Diptera are the most important insects in human parasitology, for they embrace numerous blood-sucking species that transmit the microörganisms of disease, as well as certain flies that by laying their eggs upon the surface of the human body, in wounds, or in the body openings (the nose, ears, mouth, etc.), are the cause of disease in man, their larva giving rise to severe inflammation and destruction of tissue.

Morphology.—In certain families (Muscidæ, Sarcophagidæ) the *head* shows an anterior depressed area above the antennæ, the *lunula*, which corresponds to the opening of a frontal sac (*ptilinum*) which the fly everts to force off the pupal covering. The *mouth parts* consist of labrum, epipharynx, mandibles, maxillæ, hypopharynx, and labium, all more or less modified in the different species. Thus in *Glossina* and *Stomoxys* the labial palpi are armed with teeth and adapted for piercing the skin.

The *thorax* is made up of three parts: prothorax, mesothorax, and metathorax, the mesothorax being developed most. Attached to the thorax are the wings, the venation of which has a special nomenclature.

The *abdomen* usually consists of nine segments, but by fusion may be reduced to two or more, especially with respect to the generative organs. The body is commonly covered with scales or hairs (Fig. 314), and is generally modest in color, being either yellowish, brownish, or blackish, depending in part upon the pigments that are present in the scales, and in part upon the reflection of light.

Life History.—The Diptera are usually oviparous, and only a few parasitic species are pupiparous; more rarely, as in *Glossina*, a larva is produced directly. The eggs are laid in water (*Culicidæ*), in decomposing matter, wounds, mucous membrane, etc. (*Muscidæ*), or in the soil, on vegetables, among rocks, etc. The larva is, as a rule, a very active grub, and may or may not have a distinct head. The pupa

may remain in the old larval skin, *coarctate* type (*Muscidæ*), or if it does not do so, the body and appendages will be closely united—*obtect* type. The imago may escape from its pupal skin through a T-shaped slit (*Orthorrhapha*) or by a circular opening (*Cyclorrhapha*).

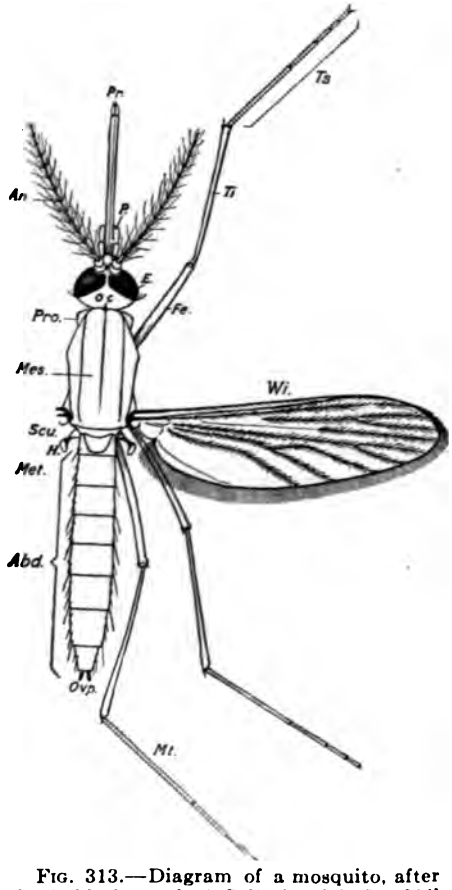


FIG. 313.—Diagram of a mosquito, after Theobald, from the "*Culicidæ of the World.*" *Pr.*, proboscis; *P.*, palp; *An.*, antenna; *E.*, eye; *Oc.*, occiput; *Pro.*, prothorax; *Mes.*, mesothorax; *Scu.*, scutellum, behind which is seen (*Met*) the shield-like post-scutellum; *H.*, haltere; *Abd.*, abdomen; *Ovp.*, ovipositor; *Wi.*, wing; *Fe.*, femur; *Ti.*, tibia; *Mt.* metatarsus; *T.S.*, tarsus—the line indicating the tarsus is made to include the metatarsus, which is sometimes regarded as the first tarsal joint. (*In Castellani and Chalmers.*)

Classification. — Following the classification adopted by Castellani and Chalmers, which is based on the character of the pupa, larva, and antennæ, and on the presence or absence of wngs, the Diptera may be divided into three suborders: I. Orthorrhapha; II. Cyclorrhapha; III. Pupipara.

I. ORTHORRHAPHA. — Diptera having no lunula; larvæ have a head; pupa is obtect; imago escapes through a T-shaped opening. It contains two divisions: (1) *Nematocera* and (2) *Brachycera.*

Division 1. *Nematocera.*— Antennæ have more than six joints, all being similar except the first two, which are without *arista;* palpi are four- or five-jointed; the body elongated; wings long and narrow; larva often aquatic. This division is subdivided into the following families: Culicidæ, Simulidæ, Chironomidæ, Psychodidæ, Blepharoceridæ, etc., each containing several genera and many species.

Division 2. *Brachycera.*— Antennæ are short and three-jointed, all joints being different; *arista* are usually present; the body is well developed, thick, and contracted; the wings are large and prominent, and contain certain number of veins and cells that are very characteristic, and the disposition of which is an aid to the recogni-

tion of the families and species. This suborder contains the following families: Tabanidæ, Leptidæ, Asilidæ, Empidæ, with many genera and species.

II. Cyclorrhapha.—Diptera having a lunula; antennæ have three joints and *arista;* palpi are one-jointed; mandibles are absent; maxillæ are rudimentary or absent; the abdomen contains seven or fewer segments. This suborder contains two divisions: 1. Aschiza, which embraces the family *Syrphidæ,* of which no species is known to be parasitic to man, and 2. Schizophora.

Schizophora.—Antennæ in separate hollows; arista well developed. This group includes the true flies, which are classified as follows: *Tribe* 1: *Muscidæ acalyptratæ,* in which, on account of the absence of squamæ the halteres are free and easily seen. This group is of no interest in human parasitology. *Tribe II. Muscidæ calyptratæ,* in which the squamæ are well developed and cover the halteres. This division comprises a number of families, four of which are important, namely: Œstridæ, Sarcophagidæ, Muscidæ and Anthomyidæ, with many genera and species.

III. Pupipara.—Wings rudimentary or absent; parasites of vertebrates; no "free-living" egg stage; the fully developed larvæ are passed directly from the body of the female adult and soon become pupæ. This suborder contains the following families: Hippoboscidæ, Nycteribidæ, Braulidæ, and Streblidæ, of which only the Hippoboscidæ are parasites of mammals.

I. ORTHORRHAPHA

DIVISION I. NEMATOCERA. FAMILY CULICIDÆ

The Culicidæ are characterized by the presence of a long, piercing proboscis; antennæ ornamented with hairs or plumes that are well developed in the male but more scanty in the female; wings having six or seven longitudinal veins and two forked cells. The body and wings are covered with scales. Metamorphosis is complete. This family is of great importance since it contains species of mosquito that are the transmitters of malarial fever, filariasis, yellow fever, dengue, and probably other protozoan and bacterial diseases.

Morphology.—*The males are easily recognized, and are differentiated from the females by the presence of antennæ which are commonly well provided with hairs.*

The Head.—The most prominent parts of the head are the proboscis, the antennæ, and the eyes. The *proboscis,* or mouth parts, consists of a labrum or upper lip, which, combined with the epipharynx, forms the labrum-epipharynx; two mandibles or cutting parts (absent in the male); two maxillæ; the hypopharynx; the proboscis sheath

(formed by the labium), which encloses the other mouth parts when the insect is not biting. The antennæ are prominent, and in the male are provided with numerous hairs or plumes. The *eyes* are conspicuous and reniform in shape. The head is separated from the thorax by a narrow but distinct neck.

The Thorax.—This consists of three parts: prothorax, mesothorax, and metathorax, of which the mesothorax is the largest.

The Abdomen.—This is made up of eight segments, with seven or eight spiracles at the sides. The last segment contains the external genital organs, which, in the male, consist of a pair of basal lobes end-

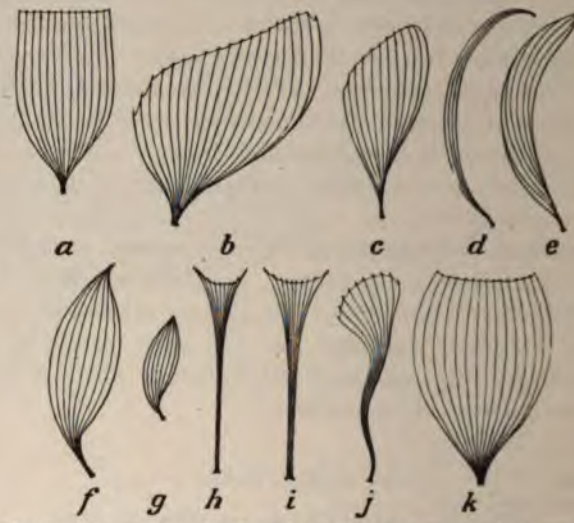


FIG. 314.—Various forms of scales found on different parts of a mosquito. (*After Theobald, from the "Culicidæ of the World."*)

a, Flat scale from abdomen; *b*, broad wing scale; *c*, another broad wing scale; *d*, curved hair-like scale; *e*, narrow curved scale; *f*, flat spindle-shaped scale; *g*, small form of *f*; *h* and *i*, upright forked scales; *j*, twisted upright scale; *k*, inflated scale. (*After Castellani and Chalmers.*)

ing in a clasp segment armed with a claw, thus forming the clasper for holding the female during copulation. The abdomen may be hairy, homogeneous in color or ringed, and in the female it is provided with flap-like ovipositors.

The legs, as in all insects, are six in number, and are composed of five segments: *coxa*, *trochanter*, *femur*, *tibia*, and *tarsus*, the last consisting of five articulations, the terminal ones being provided with equal or unequal claws, according to the species. The legs may be homogeneous in color or ringed.

The wings are two in number and arise from the mesothorax. The anterior border of the wing is straight and thick, whereas the posterior border is curved. They are covered with a certain number of veins

or nerves, separated by spaces or *cells*, and may be provided with markings or spots, the number and disposition of which are the basis for the classification and identification of the species.

The Scales.—The body of the mosquito is covered with scales, which are variable in size and shape—the size, structure, and shape are sometimes employed as a basis for classification (Fig. 314).

The Digestive Tract.—The digestive tract consists of the following parts: A *mouth*, situated at the point of fusion of the mouth parts; a *buccal cavity*, lined with chitin and extending from the mouth to the valve between it and the pharynx (this valve prevents the return of fluid to the mouth during pumping, and is more highly developed in the female than in the male); a *pharynx*, situated between the buccal cavity and the esophagus. The pharynx is provided with three chitinous plates, to which powerful muscles are attached. When these muscles contract, the pharynx becomes almost circular, and when

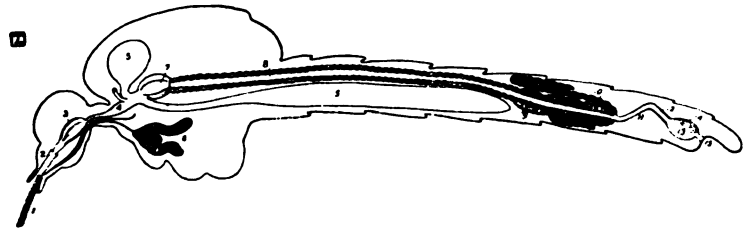


FIG. 315.—The alimentary canal of Anopheles maculipennis in situ. (*After Nuttall and Shipley, Journal of Hygiene.*)

1, Proboscis; 2, buccal cavity; 3, pharynx; 4, esophagus; 5, esophageal pouches; 6, salivary glands; 7, proventriculus; 8 and 9, mid-gut; 10, Malpighian tubes; 11, ileum; 12, colon; 13, rectum; 14, rectal papillæ; 15, anus. (*After Castellani and Chalmers.*)

they relax, the walls come together. Thus the pharynx serves as a pumping apparatus that pumps the blood of the victim through the proboscis into the stomach of the mosquito.

The Esophagus.—The esophagus is short and extends from the pharynx to the esophageal valve or proventricle, which closes the lumen of the gut when the latter contracts. It is lined with chitin, and several muscles are attached to it. The esophagus is narrow anteriorly, but expands posteriorly to form a crop-like dilatation. This posterior end of the esophagus lies on a level with the first pair of legs, and at this point gives off three pouches or diverticula—two dorsal and one ventral.

The Middle Gut or Stomach.—This is a straight tube that extends from the esophageal valve, situated at the level of the first pair of legs, to the posterior border of the sixth abdominal segment. It consists of one anterior narrow portion and a posterior more distended part or the stomach proper. The middle gut is continued by the hind-

gut, which is made up of the *intestine*, *colon*, *rectum*, and *anus*. The wall of the stomach consists of—(1) An internal cuticle; (2) a layer of epithelial cells; (3) a basement membrane; (4) a muscular coat (two layers), and (5) a serous membrane.

The Malpighian Tubes.—These are five in number; their distal ends float free in the celomic cavity, and the other ends open into the digestive tract.

The Salivary Glands.—The salivary glands are two in number, and are situated on each side of the alimentary tract, in the anterior part of the thorax, and extending as far back as the proventricle. Each gland consists of three lobes or acini—two lateral, which secrete the saliva and a middle smaller lobe which is believed to secrete a poisonous fluid. The ducts of each of these glands unite to form a single duct, which passes forward through the neck into the head. They unite in a common salivary duct at the level of the subesophageal ganglion, and end in the salivary pump at the base of the hypopharynx. These glands are not, therefore, directly connected with the alimentary tract.



FIG. 316.—Salivary gland of mosquito.

The Reproductive Organs.—The reproductive organs in the *female* consist of two ovaries and oviducts, which unite to form a common duct; a mucous gland; a spermotheca, and a genital opening. In the *male* the reproductive organs consist of testes, vasa deferentia receptaculum seminis, ejaculatory duct, and penis.

Habitat and Geographic Distribution.—In the adult stage the Culicidæ are terrestrial and aërial in habit, and live in the woods, on the shores, or along the sides of rivers, ponds, swamps, etc. The larvæ are aquatic. Certain species of mosquitos prefer to live near to or within houses. Mosquitos are cosmopolitan, being especially common in tropical regions, where they are found at all seasons of the year, although they are not infrequently seen in temperate and northern regions, where thay appear in large numbers during the summer months. Mosquitos generally bite during the night, but they may suck blood also during the day.

The Bite.—With the exception of certain males (*Stegomyia calopus*) which may occasionally attack man, only the female feeds on blood for the nutrition of the eggs, but both sexes may obtain their nutriment from the juice of vegetables. According to Manson, the female mosquito bites not only mammals, but also birds, reptiles, fish, and other insects. A mosquito becomes engorged with blood in from one to

three minutes, depending on whether the location of the bite is more or less favorable. Before biting, the insect examines the region with the palpi or with the end of the proboscis, and having selected a given area of the skin, moves the palpi away from the proboscis dorsally. The labium is now pressed against the skin, and is bent into a bow or angle posteriorly. The opening in the skin is then made by the mandibles and maxillæ, the latter working like saws, with a rocking motion of the head of the mosquito from side to side. The blood is drawn up into the stomach through a tube formed by the labrum-epipharynx, in close apposition to the hypopharynx and labrum, and by the suctorial action of the pump-like pharynx.

During the bite an irritating substance is injected under the skin by the mosquito, which brings more blood into the particular area of the skin affected, and thus enables the mosquito to obtain its supply quickly. The chemical nature of this substance is not known, but it is probably derived from the esophageal diverticula and not from the salivary gland (Schaudinn). In these diverticula fungi and bacteria are commonly found, and it is possible that this substance is an irritant produced by these microörganisms.



FIG. 317.—Anopheles in the act of biting.

Shortly after being bitten, there is an itching sensation in the affected part of the skin. On examination the area is seen to be congested, and at times a papule, or even a nodule, may form at the site of the bite. Scratching of the part may lead to secondary bacterial infection and suppuration. The itching may be relieved by the application of a diluted solution of ammonia, a 5 per cent. solution of phenol, or 95 per cent. alcohol.

Life History.—Shortly after the female hatches it becomes fertilized by the male, which dies soon after copulation. The adult female, after feeding several times upon blood, deposits the eggs in water, where they undergo development. The mosquito passes through a complicated life-cycle, which includes the egg, the larval and the pupal stage, the last giving birth to the perfect insect or imago.

The Eggs.—The eggs of *Anopheles* are laid singly upon the surface of the water, where they may be seen arranged in stars, rows, or triangles. The eggs of *Stegomyia calopus* are laid singly on the surface of water, or more often a short distance above the water, on the side of the pool or container. The eggs of *A. maculipennis* are from 0.5 to 1 mm. in length, and have a flat upper and a convex lower surface, one end being broader than the other. This broad end corresponds to the head of the future larva. A chitinous capsule or air-chamber is situated on each side of the middle third, by means of which the egg

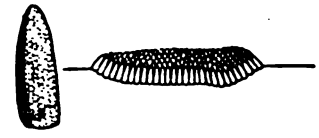
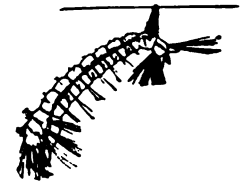
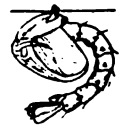
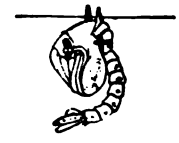
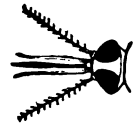
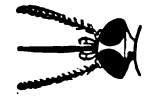
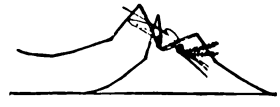
Anopheles	*Culex, Aëdes,* etc.
	
EGGS	
Eggs laid singly on surface of water; provided with a partial envelope, more or less inflated, acting as a "float."	Eggs laid in rafts or egg-boats, or singly on or near water, or where water may accumulate; never provided with a "float."
	
LARVÆ	
Larvæ have no long breathing tube or siphon; rest just under surface of water and lie parallel with it.	Larvæ have distinct breathing tube or siphon on 8th segment of abdomen; hang from surface film by this siphon, except in *Mansonia*, which obtains air from aquatic plants.
	
PUPÆ	
Pupæ have short breathing trumpets; usually do not hang straight down from surface of water.	Pupæ have breathing trumpets of various length; often hang nearly straight down from surface of water.
	
HEADS OF ADULTS	
Palpi of both male and female long and jointed, equaling or exceeding the proboscis in both sexes.	Palpi of female always much shorter than proboscis, those of male usually long, but sometimes short.
	
RESTING POSITION OF ADULT	
Adult rests with body more or less at angle with surface, the proboscis held in straight line with body.	Adult usually rests with body parallel to surface, though sometimes at an angle. Proboscis not held in straight line with body, giving "hump-backed" appearance.

FIG. 318.—Comparative table showing in a graphic way how *anopheles* may be distinguished from other common mosquitoes, such as culex. (*After Chandler.*)

floats on the surface of the water. The eggs of *Culex pipiens* are laid in masses, arranged in the form of a boat or a raft. Under favorable temperature conditions the egg hatches a larva in two or three days.

The Larva.—The larva is clearly differentiated into a head, neck, thorax, and abdomen, and in *Culex*, it is provided, on the eighth abdominal segment, with a long, stigmatic siphon for respiration, whereas in *Anopheles* the stigmata are situated at the side of the abdomen. The *head* contains the antennæ, two compound eyes, and two ocelli, the clypeus, and the mouth parts, which consist of two large feeding brushes, two mandibles, two maxillæ with palpi, and a labium (*mentum*). The *thorax* is large and set with numerous hairs. The *abdomen* is made up of nine segments provided with hairs, which in Anopheles help to maintain the larva in its horizontal position when it floats on the surface of the water. The larva is provided with a complete digestive tract and a tracheal system with ramifications all through the body. The larva of *Anopheles* thrives best in water that is



FIG. 319.—Pupa of *Anopheles maculipennis*. Nymph shortly before emerging. (*After Brumpt.*)

relatively clean, but the larva of *Culex* may develop in almost any kind of water. The larvæ of both live in fresh water, but may also be found in brackish or sea-water. The author repeatedly saw, in Brioni, larvæ of *Anopheles maculipennis* growing in sea-water. The duration of the larval stage varies from ten to eighteen days, according to the surrounding food and temperature conditions. In the temperate zone the larval stage of *Culex pipiens* lasts about twelve days, and that of *Anopheles maculipennis* from eighteen to twenty-one days. After several moltings the larva becomes a pupa.

The Pupa.—The pupal stage (Fig. 319) is very short, lasting only about forty-eight hours. During this stage no food is taken. The pupæ of all Culicidæ roughly resemble in form a question mark (?), and in addition can be recognized by the presence of two respiratory tubes on the thorax. The pupa of *Anopheles maculipennis* is straighter and more apt to lie parallel to the surface of the water.

The Imago.—Toward the latter part of the afternoon the pupa comes t the surface of the water, and the dorsal surface of the thorax splits with a T-shaped fissure, through which the mosquito escapes.

The thorax makes its appearance first, and is followed in succession by the head, the legs, and the abdomen, the entire process consuming about fifteen minutes. The insect crawls to the nearest object for support, or rests upon the old skin, and after from thirty minutes to one hour, when the wings are dried and expanded, it is able to fly. The male mosquito usually escapes first, and after copulation dies. Experimentally the female mosquitos may be induced to bite within twenty-four hours after reaching maturity, but under normal condition this probably occurs after two or more days.



FIG. 320.—Pupa of Culex fatigans. (*After Manson in Brumpt.*)

The adult *Culex* and *Anopheles* can be differentiated by their posture. When at rest, the body is bent, with the abdomen curved toward the surface of the object. The body of *Anopheles* is straight and inclined at an angle of about 45 degrees. In addition, the wings of *A. maculipennis* are provided with four characteristic black spots.

Classification.—According to Theobald, the family Culicidæ is divided into ten subfamilies, namely: (1) *Anophelinæ;* (2) *Culicinæ;*



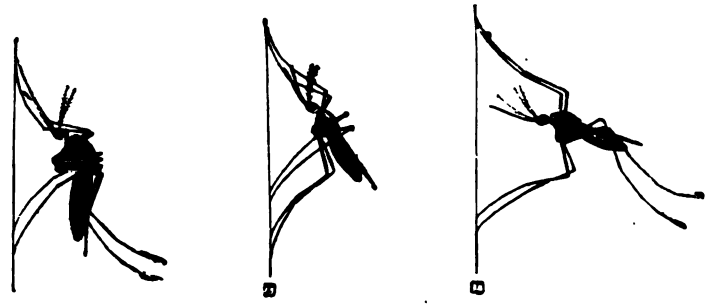
FIG. 321.—Anopheles maculipennis. Nymph emerging. (*After Brumpt.*)

(3) *Edinæ;* (4) *Megarhininæ;* (5) *Uranoteninæ;* (6) *Deinocerinæ;* (7) *Heptaphlebomyinæ;* (8) *Trichoprosoponinæ;* (9) *Dendromyinæ;* and (10) *Limatinæ,* of which only the first two, *Anophelinæ* and *Culicinæ,* and possibly the *Edinæ,* are of importance in human parasitology.

I. SUBFAMILY ANOPHELINÆ.—Proboscis straight; palpi long in both sexes; occiput has upright forked scales; eggs are laid singly; larva has no respiratory siphon.

DIFFERENTIAL CHARACTERISTICS BETWEEN ANOPHELES AND CULEX

	Anopheles	Culex
Eggs.....	Single; air-chambers on each side.	Arranged in rafts; no air-chamber on the side.
Larva.....	Absence of stigmatic siphon. Larva lies horizontal, parallel to the surface of the water.	Presence of stigmatic siphon. Larva hangs obliquely to the surface of the water.
Pupa.....	Body straight and horizontal, and parallel with the surface of the water.	Body bent like a question mark (?) and hangs downward from the surface of the water.
Imago.....	When at rest, the body lies straight and projects at an angle of about 45 degrees from the plane surface.	Body bent toward the plane surface.



A B C

FIG. 322.—Diagram showing the posture of a mosquito at rest. *a*, Culex pipiens; *b*, Myzorhynchus pseudopictus; *c*, Anopheles maculipennis. (*After Manson in Brumpt.*)

This subfamily contains the species that are known to transmit malarial fever. The following list is that given by Theobald: *Anopheles maculipennis; A. bifurcatus; Myzomyia listoni; M. culicifacies; M. funesta; M. superpicta; Myzorhynchus paludis; M. barbirostris; M. pseudopictus; M. sinensis; M. coustani; Pyretophorus costalis; Nyssorhynchus lutzi; N. theobaldi; N. stephensi; Cellia argyrotarsis; C. albimanus,* to which *Anopheles punctipennis* may be added.

Genera.—This subfamily contains several genera, of which *Anopheles, Myzomyia, Pyretophorus, Myzorhynchus, Nyssorhynchus,* and *Cellia* are the most important.

II. SUBFAMILY CULICINÆ.—Proboscis straight; palpi long in the male and short in the female; antennæ have 14 joints; wings not usually spotted; eggs generally laid in rafts; larva has a respiratory siphon.

Genera.—This subfamily contains the two important genera, *Culex* and *Stegomyia,* and perhaps a third, *Mansonia.*

I. Subfamily Anophelinæ (Theobald, 1901)

Genus Anopheles (Meigen, 1818)

The body is covered with large lanceolate scales; wings with or without spots; palpi in the female are slender and short. This mosquito is of a fairly large size. The type of the genus is ***Anopheles maculipennis.***

1. Anopheles maculipennis (Meigen, 1818).—The entire length of the insect, including the proboscis, is 7.5 to 10 mm.; wings are spotted; first submarginal cell is very large; large lanceolated scales; head has forked scales.

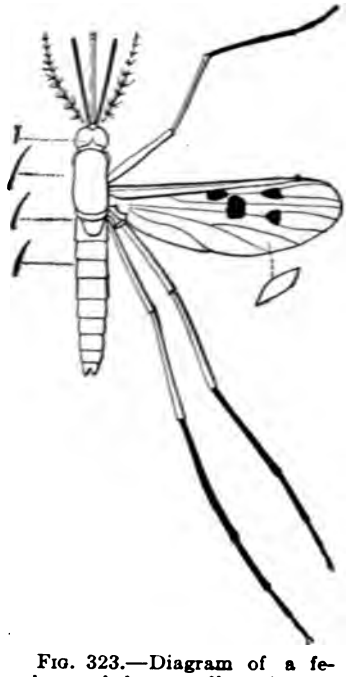


Fig. 323.—Diagram of a female anopheles maculipennis. (× 6 *after Sergent in Brumpt.*)

Habitat.—This mosquito is widely distributed; it is found in Africa, Europe, and America. The most common *Anopheles* in the northern United States is *A. punctipennis. A. maculipennis* is an old world species. The mosquito identified in the United States as *A. maculipennis* is not believed to be a different species (*A. quadrimaculatus*).

Pathogenesis.—This species is the chief carrier of malarial infection in Europe, Africa, and America. It does not transmit the *Filaria bancrofti.*

2. Anopheles bifurcatus (Linnæus, 1758).—This species is slightly smaller than *A. maculipennis*, from which it is also differentiated by the absence of spots on the wings and by the presence on the abdomen of hairs of a golden hue. The second forked cell is larger than one-half of the first.

Habitat.—Europe.

Pathogenesis.—It is the carrier of malarial infection in Europe.

Some of the other species of *Anopheles* that transmit malarial fever are:

A. formosaensis, found in Japan, and **A. tarsimaculata,** seen in Panama, etc.

Genus Myzomyia (Blanchard, 1902)

These mosquitos are generally small or of medium size; the body is covered with scales; the wings are usually spotted, and the proboscis

is unbanded. The genus embraces some species that carry malarial fever in Africa, Ceylon, and India. The type of the genus is *Myzomyia rossi.*

1. **Myzomyia superpicta** (Grassi, 1899).—This mosquito, including the proboscis, is about 7 to 8 mm. in length; the first submarginal cell is large; the abdomen is set with hairs; the legs are banded with white rings on the tarsus and the antennæ are also banded with white rings; the wings have four black spots anteriorly and several supplementary spots at the base.

Habitat.—Europe, Africa, and Palestine.

Pathogenesis.—It transmits malarial fever and serves as the intermediate host of *Filaria immites,* of the dog.

2. **Myzomyia funesta** (Giles, 1900).—This mosquito is of small size, measuring 3 to 4 mm. in length; the first submarginal cell is large; the head has forked scales; the legs have faint apical bands, and the wings are set with small scales, long and narrow, or slightly lanceolated.

Habitat.—Widely distributed throughout Africa.

Pathogenesis.—This mosquito is a common intermediate host of the malarial parasite in Africa.

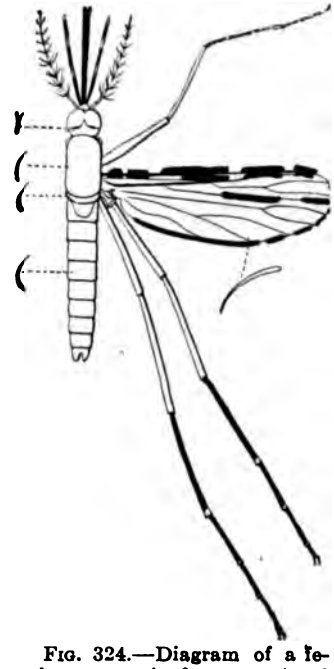


FIG. 324.—Diagram of a female myzomyia funesta. (× 6 *after Sergent in Brumpt.*)

Other species that are transmitters of malaria are:

3. **M. rossi** (Giles, 1899).—Wings with five or six pale costal spots, the largest T-shaped. India and Celebes.

4. **M. culicifacies** (Giles, 1901).—Two fringed spots. India.

5. **M. turkhudi.**—Apex of a pale black color and narrow. India.

Genus Pyretophorus (Blanchard, 1902)

Mosquitos of medium size; head set with forked scales; palpi in the female moderately provided with scales and three white bands; thorax has flat, spindle-shaped scales; abdomen is covered with hairs, but no scales; wings are freely spotted and set with small lanceolated scales. The type of the genus is *Pyretophorus costalis* (Fig. 325).

1. **Pyretophorus costalis** (Loew, 1866).—This species is from 2 to 6 mm. in length; the first submarginal cell is large; the legs are spotted and banded; three palpal bands; thorax has flat, spindle-shaped scales

the abdomen is covered with yellow hairs; the head has forked scales, and the wings have several costal black spots.

Habitat.—South and Central Africa.

Pathogenesis.—Transmitter of malrial fever and filariasis.

2. **P. jeyporensis** (James, 1902).—Apical palpal band broad; other two small. Transmitter of malarial fever in India, etc.

Genus Myzorhynchus (Blanchard, 1902)

These mosquitos are more commonly found in the open than in houses. The palpi are banded or unbanded, and the legs are banded;

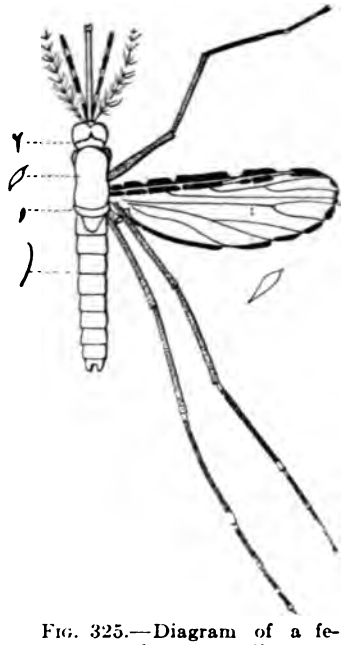


FIG. 325.—Diagram of a female Pyretophorus costalis. (× 6 *after Sergent in Brumpt.*)

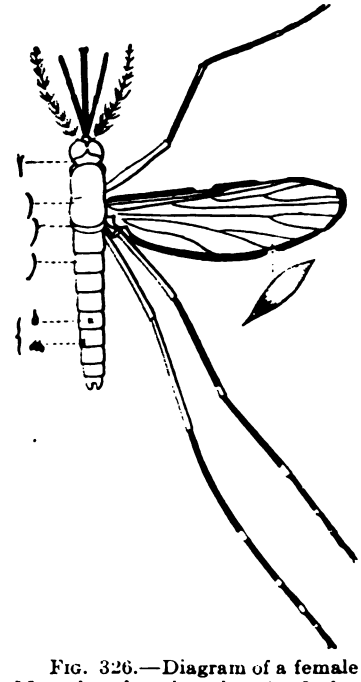


FIG. 326.—Diagram of a female Myzorhynchus sinensis. (× 6 *after Sergent in Brumpt.*)

thorax is set with curved, hair-like scales; wings have lanceolated scales. The type of the genus is *Myzorhynchus sinensis.*

1. **Myzorhynchus pseudopictus** (Grassi, 1899).—This species is large —about the size of *Anopheles maculipennis* (9 to 10 mm. in length); first submarginal cell is large; palpi have four pale bands; apex is white; thorax and abdomen have curved, hair-like scales; wings are without prominent spots and are ornamented with lanceolate scales; last hind tarsal brown in color.

Habitat.—Central and southern Europe.

Pathogenesis.—Transmits malarial fever.

2. **M. sinensis** (Wiedemann, 1828).—Wing-fringe has one pale spot. Transmitter of malarial fever and filariasis in Japan.

3. **M. paludis** (Theobald, 1900).—Last three hind tarsals white. Transmitter of malarial fever in Africa.

4. **M. barbirostris** (Van der Wulp, 1884).—Legs not spotted. Transmitter of filariasis and malarial fever in the Orient, etc.

Genus Nyssorhynchus (Blanchard, 1902)

Palpi thickly set with scales; thorax has fusiform and narrow curved scales; wings are spotted and set with large lanceolate scales; legs are commonly banded. The important species of the genus is *N. fuliginosus* (Giles, 1900), which is a carrier of malarial fever.

1. **Nyssorhynchus theobaldi** (Giles, 1901).—Three white palpal bands, the two apical being close together. Transmitter of malarial fever in India.

2. **N. stephensis** (Liston, 1901).—Legs spotted, proboscis dark. Transmitter of malarial fever in India.

3. **N. fuliginosus** (Giles).—Wings have four white costal spots. Carrier of malarial fever, etc.

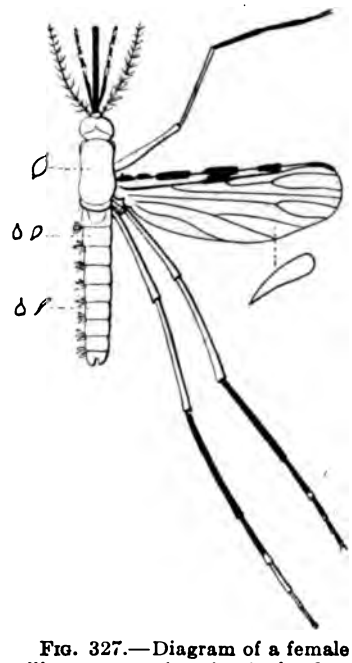


FIG. 327.—Diagram of a female cellia argyrotarsis. (× 6 *after Sergent in Brumpt.*)

Genus Cellia (Theobald, 1902)

This genus is found widely distributed in the tropics; antennæ and palpi are set with dense scales; the abdomen is covered with irregular scales, the thorax with flat and fusiform scales, and the wings with large lanceolate scales. The type of the genus is *Cellia argyrotarsis.*

1. **Cellia argyrotarsis** (Robineau-Desvoidy, 1827).—This species is found widely distributed in Central and South America, where it transmits malarial fever and filariasis. Color dark; legs with last three hind tarsals white.

2. **C. pharoensis** (Theobald, 1901).—Femur and tibia not mottled; apical foot-bands. Transmitter of malarial fever in Africa.

3. **C. albimanus** (Wiedemann, 1821).—Legs with last hind tarsal white; second and third white. Carrier of malarial infection and filariasis in Central and South America.

4. **C. brasiliensis** (Chagas).—Carrier of malarial fever in Brazil (?), etc.

II. Subfamily Culicinæ (Theobald, 1902)

Genus Culex (Linnæus, 1758)

Proboscis straight; palpi long in the male, and short in the female; wings with long first submarginal cell; third anal vein absent; larva has respiratory siphon; head has narrow curved scales above and flat on the side; thorax has hair-like or narrow curved scales. The important species are *Culex pipiens* and *C. fatigans*.

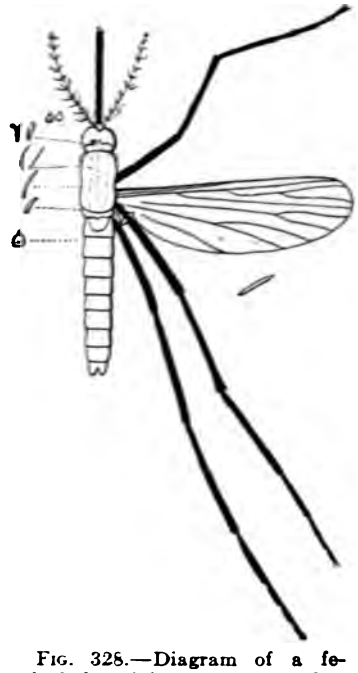


Fig. 328.—Diagram of a female Culex pipiens. (× 5 *after Sergent in Brumpt.*)

1. **Culex pipiens** (Linnæus, 1758). **This species is the common brown mosquito of Europe, North Africa, and North America. The thorax is dark brown, and set with golden-brown curved scales and three dark lines. Wings have no spots, and are set with straight scales; first submarginal cells large; abdomen brown, with basal yellow bands and flat scales; legs unbanded. This mosquito is of medium size, *i.e.*, 4 to 6 mm. in length.**

Habitat.—Cosmopolitan.

Pathogenesis.—It transmits the *Filaria bancrofti*, malarial fever in birds and probably Malta fever.

2. **Culex fatigans** (Wiedemann, 1838).—This is the common house mosquito of the tropics. It resembles *C. pipiens*, from which it is differentiated by the presence of but two dark lines in the thorax; and the fact that the basal abdominal bands are lighter, and the first forked cell longer.

Pathogenesis.—It transmits filariasis and dengue.

Other species are *Culex skusei* (Giles); *C. gelidus* (Theobald); *C. sitiens* (Wiedemann), and *C. albolineatus;* all are transmitters of *Filaria bancrofti.*

Genus Stegomyia (Theobald, 1901)

These insects are dark brown in color; the head is set with flat scales; proboscis straight; palpi short—about one-third the length

of the proboscis in the female, but long in the male; thorax is covered with fusiform or curved, hair-like scales; the abdomen is covered with flat scales, banded or unbanded, but marked with white spots at the side; the wings resemble those of Culex but are smaller; eggs are deposited singly; the larva is provided with a respiratory siphon. The type of the genus is *Stegomyia calopus*.

1. **Stegomyia calopus** (Meigen, 1868) (*S. fasciatus, Culex fasciatus*).—In addition to the characteristics of the genus just described, this species is distinguished by the presence of two pale, parallel, longitudinal lines in the middle and two curved lines on each side of the thorax; the abdomen is dark and hairy, and has basal bands and lateral patches, which are white in color; hence the name, "tigre mosquito," commonly given to it; the legs are dark brown and have white basal rings; the proboscis is unbanded. Larva has a head of the same size as the thorax.



FIG. 329.—Stegomyia calopus, female. (*After Manson in Brumpt.*)

Habitat.—This species is widely distributed. It inhabits, by preference, swampy localities and the banks of rivers. It bites chiefly at night, except shortly after hatching, when still very young, when it bites during the day. According to Finlay, this insect does not bite when the surrounding temperature is below 23°.

Pathogenesis.—This mosquito is the transmitter of yellow fever. It becomes infected only when it bites a yellow fever patient during the first three days of the disease, but may conserve the virus and be infective for over two months.

2. **S. scutellaris** (Walker).—Legs and abdomen are basally banded; thorax has one median silvery white line. It transmits *Filaria bancrofti*.

Genus Mansonia(?) (R. Blanchard, 1901)

Head has narrow curved scales; antennæ are short, with 14 segments in the female and 15 in the male; proboscis short; thorax covered with curved, hair-like scales, and the abdomen with flat scales. The eggs are bottle-shaped and laid singly. Larva and pupa are not known.

1. **Mansonia uniformis** (Theobald, 1901).—This species is found in Africa and Asia and is the transmitter of *Filaria bancrofti.*

2. **M. annulipes** (Theobald, 1901).—Transmits *Filaria bancrofti.*

DIVISION II. BRACHYCERA. FAMILY TABANIDÆ

The family Tabanidæ comprises flies of fairly large size, and characterized by a broad flat body and a large head, with prominent eyes that meet at the back in the male but are somewhat separated in the female (Fig. 330). The third joint of the antennæ is marked by three or seven annuli. The proboscis is well developed and adapted



FIG. 330.—Tabanus bovinus (female). (*After Castellani and Chalmers.*)

for piercing. The thorax is narrower than the head. When the fly is at rest, the wings diverge at the tip and are separated. This serves as a point in differentiating it from the genus *Musca*, in which the wings are partially closed and only slightly overlap one another, and from the genus *Glossina*, in which both wings completely overlap, presenting a tongue-shaped appearance—hence the name. The legs are large and strong. The body is brown or black in color, and with or without markings on the abdomen.

Life History.—The eggs are spindle-shaped and brown or black in color. They are laid in rafts or masses on aquatic plants or stones. The larva (Figs. 332, 333) is spindle-shaped and segmented, with knobs on the rings. It lives in water, damp soil, or as a parasite on other larvæ, and feeds upon small animals. The pupa (Fig. 332) is free and is found in water or in the soil. The adults are blood-sucking

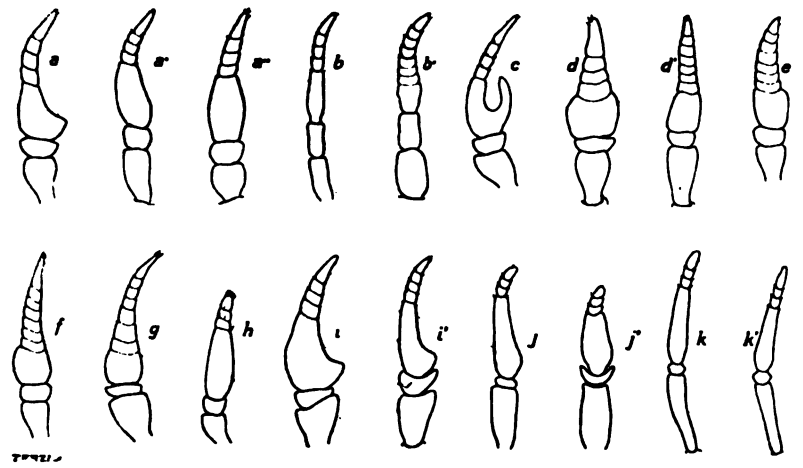


FIG. 331.—Antennæ of the Tabanidæ. *a*, *a'*, *a''*, silvius; *b*, *b'*, chrysops; *c*, rhinomyza; *d*, *d'*, cadicera; *e*, dorcaloemus; *,* pangonia; *g*, erephopsis; *h*, lepidocelaga; *i*, *i'*, tabanus; *j*, *j'*, hematopota; *k*, *k'*, hippocentrum, (*After Castellani and Chalmers.*)

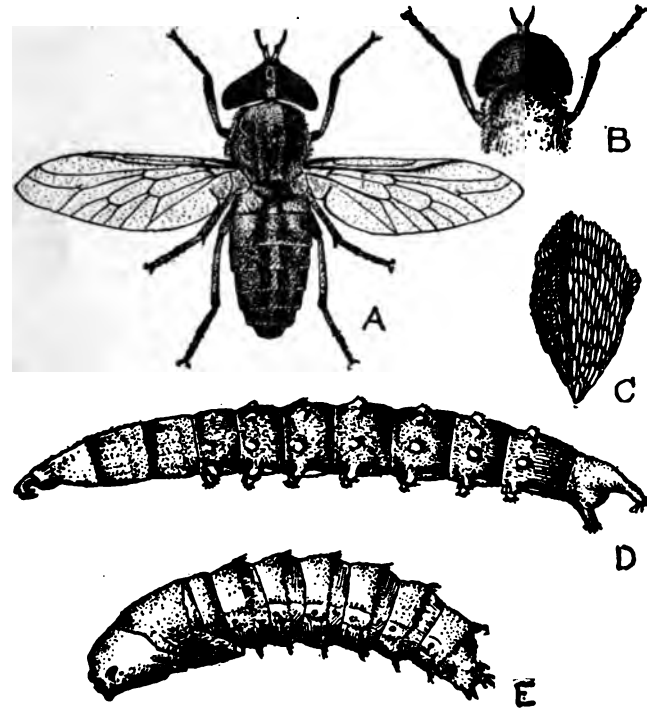


FIG. 332.—Life history of a tabanid, Tabanus kingi, a "seroot" of Sudan. *A*, adult female, × 3; *B*, head of adult male, × 3; *C*, egg mass, laid in crevices of rock, × 5; *D*, larva, × 2½; *E*, pupa, × 2½. (*After King in Chandler.*)

flies, of which from 1500 to 2000 species have been described. They are distributed widely throughout the world, and are variously known as horseflies, breeze-flies, gadflies, serut-flies, mangrove-flies, etc. Only the females feed on blood. The males live on the juices of plants. The Tabanidæ are wont to come to water to drink, a point that has a practical application in prophylaxis, since they can easily be destroyed in great numbers by sprinkling the water with petroleum.



FIG. 333.—Larva of an African Tabanidæ. *A*, dorsal and *B*, ventral view; *C*, schematic transverse section across the middle of a segment. (× 4 *after Brumpt.*)

Pathogenesis.—The Tabanidæ are of great importance in veterinary medicine, since they are the transmitters of pathogenic trypanosomes in animals. Their importance in human parasitology has not, however, been demonstrated. They are believed to transmit *Filaria loa* and possibly some protozoan parasites.

Prophylaxis.—The sprinkling of the water about the places where these insects live with petroleum, is the best method of exterminating these flies.

Classification.—The family Tabanidæ is divided into two subfamilies: I. *Tabaninæ;* II. *Pangoninæ.*

SUBFAMILY I. TABANINÆ.—These insects are characterized by the absence of spurs on the posterior tibia. The subfamily comprises five genera: *Tabanus; Lepidoselaga; Hematopota; Therioplectes,* and *Atylotus,* with many species.



FIG. 334.—Nymph of Tabanus bromius, male. (*After Surcouf and Ricardo in Brumpt.*)

SUBFAMILY II. PANGONINÆ.—These are characterized by and differentiated from *Tabaninæ* by the presence of spurs in the hind tibia. The subfamily comprises four genera: *Pangonia, Chrysops, Silvius,* and *Cadicera,* with many species.

SUBFAMILY I. TABANINÆ

Genus Tabanus (Linnæus, 1761).—The body is generally large; tubercle at base of antennæ is absent, but the third joint has a well-

developed basal tooth. The genus contains over 900 species, of which *T. bovinus*, the "gadfly" of cattle, is found in Asia, Europe, and South Africa. *T. ditæniatus*, *T. gratus*, *T. jasciatus*, etc., called "serut-flies," are found in the Sudan; *T. atratus* is the common black "horse-fly" of North America, etc.

Genus Lepidoselaga (Macquart, 1838).—The body is covered with scales having a metallic, glistening appearance. *L. lepidota* is the common "motuca fly" of Brazil.

Genus Hematopota (Meigen, 1803).—Absence of basal tooth on the third joint of the antennæ, which is well separated from the second joint. The genus contains over 60 species. *H. pluvialis* and *H. italica* are the common European species. Several species are found in Africa, of which *H. abseura* is found in South Africa.

Genus Therioplectes (Zeller, 1842).—Several species of this genus, *T. micans*, *T. borealis*, etc., are found in Europe.

Genus Atylotus (Osten-Sacken, 1876).—*Atylotus fulvus*, *A. rusticus*, etc., are found in Europe.

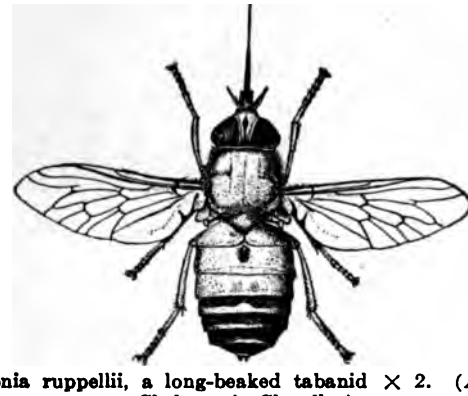


FIG. 335.—Pangonia ruppellii, a long-beaked tabanid × 2. (*After Castellani and Chalmers in Chandler.*)

SUBFAMILY II. PANGONINÆ

Genus Pangonia (Latreille, 1802).—This genus can be recognized by the size of the proboscis, which is much longer than the head, and sometimes longer than the body. The genus comprises several species, such as *P. rostrata*, *P. varicolor*, etc., common in Africa and other species found in various parts of the world.

Genus Chrysops (Meigen, 1803).—This genus can be recognized by the size of the second joint of the antennæ, which is smaller than the first; the palpi are slender and slightly curved; the wings are usually provided with brown bands. The genus is widely distributed and contains about 160 species. *C. dimidiata*, *C. dispar*, etc., are common in Africa.



PLATE XIII

Larvæ of Gastrophilus equi (bot fly) attached to the mucosa of the stomach of hor

Genus Silvius (Meigen, 1820).—This genus is also cosmopolitan. *S. denticornis* is found in Africa.

Genus Cadicera (Macquart, 1855).—This genus can be recognized by the fact that the antennæ are not very prominent, and are inclined toward the base. The palpi are very large and well developed. *C. melanopyga, C. chrysostigma,* etc., are found in Africa.

II. CYCLORRHAPHA

SUBORDER SCHIZOPHORA. FAMILY ESTRIDÆ

This family is characterized by the presence of a hairy body, a prominent and spheric head provided with two eyes and three ocelli, resembling the head of a bee. The antennæ are short, and are inserted into a round pit; the mouth parts are rudimentary. The Estridæ

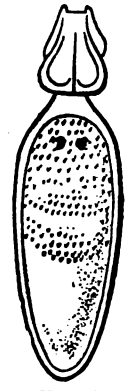


FIG. 336.

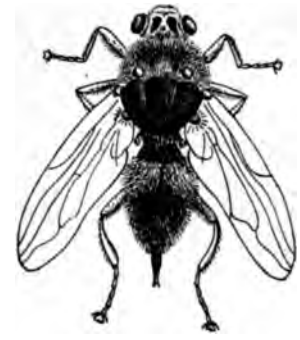


FIG. 337.

FIG. 336.—Egg of hypoderma containing a larva provided with cuticular spines. (*After Brauer in Brumpt.*)

FIG. 337.—Hypoderma bovis, female. (*After Brauer in Brumpt.*)

are commonly known as the "bot" or "warble-flies," and are of interest because of the fact that their larvæ are parasites that invade the nasal cavities or the stomach or intestines of various animals and sometimes of man. The family is divided into three genera: *Hypoderma, Gastrophilus,* and *Dermatobia.*

Genus Hypoderma (Latreille, 1825)

Body is yellowish gray or black in color, either bare or provided with hairs. Wings are transparent or brownish, and with or without bands or spots. These flies are 8 to 15 mm. in length. Proboscis is straight or rudimentary; palpi are absent.

1. **Hypoderma bovis** (De Geer, 1776).—Body is dark and covered with hairs. The thorax has three or four longitudinal dark bands. Wings are brownish and without spots. It is from 13 to 15 mm. in length (Fig. 337).

Habitat.—This fly is widely distributed, and is generally found about stables and near cattle. It is common in Europe, Africa, and America.

Life History.—The eggs are deposited on the skin of cattle and are transferred to the mouth by licking, but in some cases, at least, the larva from the egg actually burrows through the skin and passes to the esophageal region. From the esophagus the larva travels to the subcutaneous tissue and forms a tumor under the skin which is provided with a small aperture through which the larva eventually escapes. It drops to the ground, becomes a pupa, and finally develops into an adult fly.

Pathogenesis.—The larva of this fly is a parasite of cattle, but it has also been found in man.

2. **Hypoderma diana** (Brauer, 1858).—The larva of this species is longer and thinner than the larva of *H. bovis*. In the larval form it is a common parasite of goats and sheep, but has also been found in man.

Genus Gastrophilus (Leach, 1817)

Wings are without transverse veins, but a median vein runs toward the posterior border; arista naked.

Gastrophilus equi (Fabricius).—The larva is a parasite in the stomach and intestine of the horse, where it causes irritation (Plate XIII). In due course the larva is discharged with the feces and becomes a pupa in the soil.

Genus Dermatobia (Brauer, 1860)

The body is metallic gray in color; the proboscis is bent and capable of being drawn under the head. The third joint of the antennæ is longer than the other two.

Dermatobia cyaniventris (Macquart, 1840).—The adult fly is 14 to 17 mm. in length. The body has a gray, metallic sheen. The head is yellowish and the eyes are of a brilliant brown-yellow color. The wings are light brown. When young, the larva is shaped like a drumstick, with a thick anterior and a thin posterior end, at the top of which is the stigma; as it grows older it becomes club-shaped.

Habitat.—The fly is distributed widely throughout South America, and is found in the woods and pastures. The larva lives as a parasite in cattle, dogs, and at times in man.

Life History.—The female deposits the eggs in the crevices of trees in the woods, and as they are provided with a viscous liquid, they easily attach themselves to the body of mosquitos if they alight on trees. The mosquitos, in turn, transfer the eggs to the skin of any animal or man upon which they may subsequently alight. The eggs

may also, and perhaps more commonly, be deposited directly on the skin or in small wounds, where they hatch a larva that lives under the dermis and produces suppuration. Eventually the larvæ (Fig. 339, drop to the ground, where they undergo pupation.



FIG. 338.—Dermatobia cyaniventris (female). × 3. (*After Castellani and Chalmers.*)

Pathogenesis.—The presence of the larvæ beneath the skin is the source of marked irritation and inflammation that results in a furuncle-like swelling with a small opening at the center.

Treatment.—Calomel or other antiseptics introduced into the swelling through the opening in the skin is followed by good results. The introduction of oils into the swelling may bring about asphyxia of the larva.



FIG. 339.—Dermatobia cyaniventris (young larva). × 3. (*After Blanchard in Castellani and Chalmers.*)

FAMILY SARCOPHAGIDÆ

The flies of this family present the following characteristics: Body large; color dull gray, rarely iridescent; antennæ feathery or pubescent half way to the tip; legs stout. The family contains numerous genera, of which *Sarcophaga*, *Sarcophila*, and *Cynomyia* are most important.

Genus Sarcophaga (Meigen, 1826)

Antennæ feathery, except at the extremity; abdomen gray, with black and white markings.

1. **Sarcophaga carnaria** (Linnæus, 1758).—This fly can be recognized by the yellowish color of its head; dark palpi; a thorax marked with

yellowish-gray lines; an abdomen regularly marked with symmetric spots. The female measures 13 to 15 mm. in length, but the male is much smaller.

Habitat and Life History.—The species is widely distributed. The fly is viviparous, and the larvæ are usually deposited upon decomposing animal matter, where they develop into the imago. They are occasionally found in ulcers and in other lesions in man.

Pathogenesis.—The larva is an accidental parasite of man and animals, and may be found in ulcers of the skin or in the normal body cavities. Other species of interest are the following:

2. **S. magnifica** (Schiner, 1862) is found in Russia.
3. **S. chrysostoma** is found in Central and South America, etc.

Genus Sarcophila (Rondani, 1856)

Antennæ feathery, with third joint more than twice as long as the second; front large in the two sexes; abdomen whitish gray in color.

The larvæ of **Sarcophila latifrons; S. meigeni, S. ruralis,** etc., have been found in myiasis of the skin in man.

Genus Cynomyia (R. Desvoidy, 1830)

Body iridescent; wings with fourth longitudinal vein curved at right angle near the border, and terminal transverse vein concave.

Cynomyia mortuorum (Linnæus, 1761).—The larvæ of this species are sometimes found in ulcers of the skin.

FAMILY MUSCIDÆ

The members of this family present the following characteristics: The body is stout and the thorax short. Among the non-biting species (*Musca domestica*), the probosis consists of a pharyngeal tube formed by the labrum, epipharynx, and hypopharynx, whereas in the biting species (*Glossina morsitans*) this is modified for cutting, piercing, and sucking. The arista is either plumose or pectinate to the tip. The first posterior cell is either slightly opened or closed to the border of the wing. These flies are found throughout the world, but are especially abundant in the tropic and in temperate climates during the summer months. Those most common to America are: *Musca domestica* (house-fly); *Stomoxys calcitrans* (stable-fly); *Drosophila ampelophila* (dung-fly), etc. Of these, the house-fly represents about 90 per cent. The family contains several genera, of which *Stomoxys*, *Glossina*, *Musca*, *Cordylobia*, *Lucilia*, *Chrysomyia*, *Calliphora*, and *Auchmeromyia* are the most important.

Genus Stomoxys (Geoffroy, 1762)

The genus *Stomoxys* is cosmopolitan in distribution. The proboscis is adapted for biting, the palpi are slender, and about half the size of the proboscis.

Stomoxys calcitrans (Linnæus, 1761).—This fly, commonly known as the "stable-fly," bears a close resemblance to the common house-fly (*Musca domestica*), from which it is differentiated by the hairy and spotted abdomen and by the position of the head, which is held raised when the fly is at rest; it is also distinguished by the wings, which touch one another at their base and diverge behind.



FIG. 340.—Stomoxys calcitrans, female. (*After Castellani and Chalmers.*)

The mouth parts are adapted for piercing, and consist of labrum, hypopharynx, and labium. Its bite is painful.

Habitat and Life History.—This fly is common about stables. According to Newstead, the incubation period of the egg is two to three days, the growth of the larva requiring two or three weeks, and the pupal stage, consuming from nine days to two weeks, making the total period of development from three to five weeks.

The eggs are about 1 mm. in length, of a white, turning to yellow, color; they are convex on one side and straight on the other, where a groove is seen, deeper anteriorly, through which the larva escapes. The eggs, to the number of from 50 to 80, are deposited in dung or in decomposing vegetation.

The larva is about 11 mm. long, club-shaped, and tapered anteriorly; it is yellowish in color. The mouth is dark in color and is provided with a hook that is used for locomotion. The posterior stig-

mata are three in number. They are small and disposed in a triangular fashion.

The pupa is about 5 mm. in length, heart-shaped, is made up of about nine segments, and is reddish in color. Pupation takes place in about two hours.

Pathogenesis.—This fly is the recognized agent of transmission of *Trypanosoma evansi*, the cause of the disease known as "surra." It has also been accused of acting as a transmitter of *Bacillus anthracis*. The experiments of Rosenau and Anderson have tended to prove that it may transmit the virus of poliomyelitis.

There are several other species of Stomoxys, such as *S. sibiens*, *S. inornata*, *S. nigra*, *S. pusilla*, *S. limbata*, etc.



FIG. 341.—Stomoxys calcitrans. *A*, larva (× 5); *B*, pupa (× 3 *after Newstead in Brumpt.*)

Genus Glossina (Wiedemann, 1830)

The Glossina, or "tsetse-flies," present the following characteristics: Proboscis well developed and projecting horizontally forward between two well-developed palpi, which are almost or fully as long as the proboscis; when at rest the wings overlap upon the back of the insect like the blades of a pair of scissors, giving the fly a tongue-shaped appearance—hence the name of the genus, Glossina.

The eyes are prominent; the antennæ are three-jointed, the first two being smaller than the third. The thorax is somewhat triangular in shape, and distinctly constricted posteriorly, at its junction with the abdomen. The abdomen is flat and oval when empty, but globular in shape when full; it is composed of six segments. The wings are brownish in color, and have a peculiar venation.

The legs are simple and long, and are provided with claws and pulvilli. The male can be recognized by the presence of a genital groove with thickened margins on the ventral surface of the sixth segment in the median line, surrounded by a patch of dark hair on each side.

Habitat.—This genus is confined to tropical Africa and Arabia. The flies live in jungles or on bushes along the banks of streams or lakes; *G. longipennis*, however, inhabits the deserts. The flies do not, apparently make excursions beyond a radius of from 70 to 80 yards of the water, except when pursuing man or animals, when the females can be induced to travel great distances. The tsetse-fly lives chiefly

on the blood of animals and man. According to Koch, *G. palpalis* also bites the crocodile. With few exceptions, the flies bite only during the day.

Life History.—The Glossina is viviparous. The larva develops inside of the mother until it is nearly full grown, when it is deposited in moist soil—usually about the roots of trees and along streams and lake shores. The larva is reddish in color and consists of twelve segments, the anterior of which has two hooks and the posterior a dark anal segment. On being deposited, the larva immediately digs several inches into the soil and in the course of a few hours becomes a pupa.

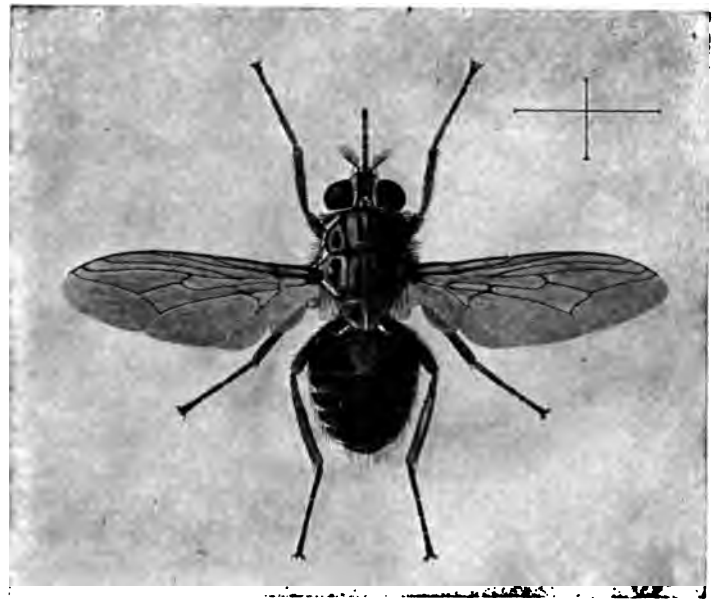


FIG. 342.—Glossina palpalis, female. (*After Castellani and Chalmers.*)

The pupa is dark in color, globular in shape, with two small expansions anteriorly. It measures 6.3 to 7 mm. by 3 to 3.6 mm. The breeding time seems to be at the beginning of the rainy season.

Pathogenesis.—The tsetse-flies (*Glossina palpalis* and *G. morsitans*) are the transmitters of *Trypanosoma gambiense* and *T. rhodesiense*, which produce sleeping sickness in man. *G. morsitans* is also the transmitter of *T. brucei*, which is the cause of "Nagana."

1. **Glossina palpalis** (Robineau-Desvoidy, 1830).—This fly (Fig. 342) has attracted considerable attention in recent years since it was found to be the transmitter of *Trypanosoma gambiense*, the cause of sleeping sickness in tropical Africa. It can be recognized by the following characteristics: Its large size, being 8 to 9 mm. in length;

dark abdomen, with pale area on the second segment, usually triangular; third joint of antennæ gray brown or cinereous black; hind tarsi blackish.

Habitat.—Central Africa, around the Congo region, and East Africa as far as the great lakes, the Nile, the southern part of Rhodesia, and southern Arabia. The fly lives in moist localities along the borders of rivers and lakes. It is diurnal, and bites only during the day, especially during the noon hour, and not so frequently at dawn or late in the afternoon. The most suitable requirements for breeding are loose ground and dry and friable earth, protected from the sun and rain by the shade of trees and underbrush, and situated not more than twenty yards from the water.

Life History.—The female deposits a larva every nine or ten days, until six or eight have been produced. It burrows its way into the ground, where it pupates in a short time and becomes an adult in about six weeks.



FIG. 343.—Larva of tsetse fly. (*Glossina palpalis.*) × 5. *After Roubaud in Chandler.*)

Pathogenesis.—*Glossina palpalis* is the transmitter of sleeping sickness in Africa. The transmission is chiefly mechanical at first, but later, according to Klein, evolution of the trypanosome takes place and is completed from ten to twenty days in the stomata of the fly, after which it remains infective for about thirty-one days. According to Bruce, Hamerton, Klein, and others, only a small percentage—about 1 in 60—of the flies become infected.

2. **Glossina morsitans** (Westwood, 1850).—This species is distributed widely throughout Central Africa. It can be recognized by the following peculiarities: The hind tarsus is not entirely dark; the last two joints of the front and middle legs have sharply defined dark brown or black tips; head is narrow.

Habitat and Life History.—These are the same as for *Glossina palpalis.* This fly is said to be more widely distributed in Central Africa than *G. palpalis,* and it is said to be especially common in Rhodesia.

Pathogenesis.—*Glossina palpalis* is the transmitter of *Trypanosoma brucei,* the cause of nagana in horses, etc. The transmission is mechanical for the first three days, after which it becomes non-infective, remaining so during the fourth to the tenth day, and becoming infective again after the eleventh day. It remains infective for over one month (Taute). According to Kinghorn, de York, and de Lloyd, *G. morsitans* is also a transmitter of *T. rhodesiense,* which is the cause of sleeping sickness in Rhodesia, a disease that is regarded by these

authors as differing from the common sleeping sickness of Central Africa.

Other species of *Glossina* that are said to transmit trypanosomes to man and animals are the following:

3. **Glossina fusca** (Walker, 1849).—Found throughout Africa; probably transmits *T. brucei* and *T. gambiense.*

4. **G. longipennis** (Corti, 1895); **G. longipalpis** (Wiedemann, 1830); **G. pallicera** (Bigot, 1891), etc., are all probably transmitters of trypanosomes to man and animals.

Genus Musca (Linnæus, 1761)

The following are some of the characteristics of this genuss Head of medium size; eyes prominent, grayish in color, almost meeting in the male, and separated in the female by a wide frontal stripe; proboscis long, soft, retractile, and elongated at the tip and adapted for licking or lapping; body brownish or dark in color, with white streaks; wings only partially folded when at rest. The type of the genus is *Musca domestica.*

These flies have for many years been regarded as carriers of pathogenic microörganisms. Celli in 1888 succeeded in demonstrating the presence of the typhoid bacillus in the excrement of a house-fly after it was fed upon a pure culture of the organism, and since that time the importance of these insects as carriers of diseases in man and animals has been recognized. At present they are regarded as capable of transmitting typhoid fever, cholera, dysentery, summer diarrhea of children, trachoma, tuberculosis, leprosy, Oriental sore, and several skin affections. In addition, the larvæ of these flies are occasionally found as parasites in ulcers of the skin, in the normal body cavities, upon mucous membranes, and in the intestinal tract. Their presence in these localities gives rise to the condition known as myiasis.

Musca domestica (Linnæus, 1751).—The house-fly is recognized by the following characteristics: Head f medium size; eyes prominent and separated in the female by a white streak. The proboscis is long, soft, and retractile, and adapted for licking, lapping, or sucking, but not for biting; it consists of the rostrum, haustellum, (proboscis proper), which constitutes the pharyngeal tube formed by the labrum, epipharynx, and hypopharynx, the hypopharynx receiving the salivary or hypopharyngeal tube. The wings are transparent, the costal and subcostal veins are well developed, and the costal and first costal cells are present. When at rest, the wings overlap anteriorly only and diverge from the base. The body is brown in color. Abdomen is made up of eight segments in the male and of nine in the female.

Habitat.—The house-fly lives by preference in or near houses, tables, butcher-shops, etc.; about garbage heaps and in decomposing:

matter about the house or in the yard. It prefers dry localities, which accounts for the fact that flies swarm in houses during a storm or in rainy weather. They also select quiet places, free from strong drafts or winds. Flies are very sensitive to dampness or rain, which usually kills them within a short time. They soon perish when subjected to confinement. The author has not succeeded in keeping flies alive for more than forty-eight hours in confinement. Under such conditions, as a rule, they refuse to feed in a few hours, and restlessly search for a means of escape until exhaustion overtakes them.

Life History.—The females deposit from 120 to 150 eggs at a time. As a rule, the eggs are deposited in human fecal matter, horse-manure,

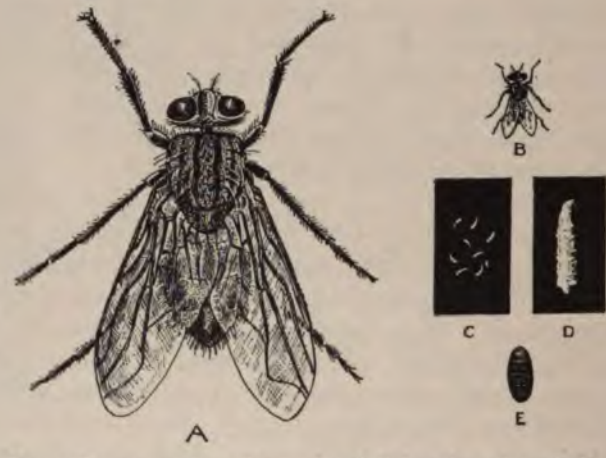


FIG. 344.—House fly, musca domestica. A, adult female, enlarged; B, natural size; C, eggs; D, larva, E, pupa.

cow-manure, garbage, and vegetables in a stage of fermentation, on which the larvæ feed when hatched. The entire life-cycle occupies from twenty-three to forty days, according to temperature and food conditions. This time is divided as follows: Egg, one to three days; larvæ, five to fourteen days; pupa, three to five days. The imago becomes sexually mature in from ten to fourteen days, and ovulation occurs four days after fertilization.

The Egg.—The egg measures about 1 mm. in length. It is oval in shape, white in color, and broader at the posterior end. The larva hatches at the dorsal portion of the anterior narrower end.

The Larval Stage.—The arva has a slender body, composed of twelve segments, and is pearl white in color. Its development is divided into three stages:

1. The first stage lasts from twenty-two to thirty-two hours. The larva is about 2 mm. in length. The anterior end is narrower and con-

tains a rudimentary head; the posterior end contains two stigmatal openings. There is a spiny area at the anteroventral edge of each segment.

2. The second stage lasts twenty-four hours; the larva develops a pair of anterior spiracles.

3. The third stage lasts from three to four days. The alimentary canal is complete. The larva grows rapidly and becomes a pupa.

The Pupa.—Pupation takes place in from three to four hours; the pupa measures 3–6 mm. It is yellowish white at first, and then becomes dark brown. This stage lasts from three to five days. The imago escapes by a circular split. Hatching takes place under ground or in rubbish. The young fly is gray at first and then becomes brown and black.

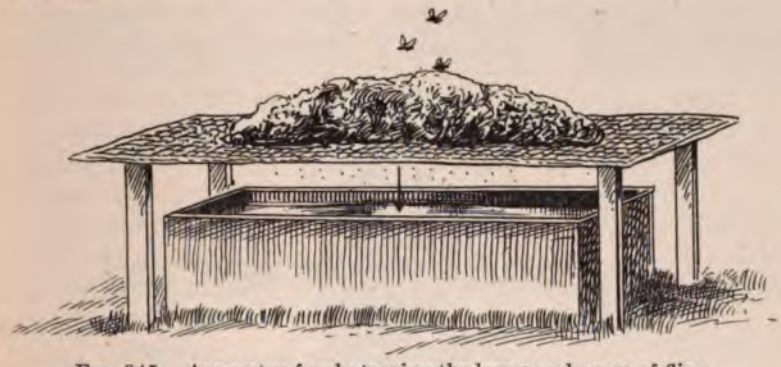


FIG. 345.—Apparatus for destroying the larvæ and pupæ of flies.

Pathogenesis.—As previously stated, the house-fly has been shown to be a carrier of the microörganisms of typhoid fever, cholera, dysentery, plague, etc., and of pyogenic bacteria. The fly may occasionally lay the egg in ulcers or wounds or in the normal body cavities, giving rise to the condition known as myiasis. In a few instances the larva has been found in the intestine.

Prophylaxis.—The use of appropriate containers for garbage, general cleanliness about houses and stables, the use of lime for disinfection, and the removal of decomposing organic matter from yards and gardens, constitute the most efficient measures against the house-fly. A very simple and efficient method for destroying the larva, especially about stables, consists in placing manure, fermenting vegetables, and the like in trenches placed over a receptacle containing water (Fig. 345). The success of the method rests on the habit of the larva of burrowing under the ground for pupation. As a result of this, the larva in making its way toward the lower part of the heap, eventually falls into the water and is drowned. Proper screening of doors and windows will prevent the entrance of this pest into houses. For immediate

destruction of the adult fly the slogan, "Swat the fly!" has borne good fruit. Fly-paper, fly-traps, and the like, are also used. The author has seen very satisfactory results follow the use of a preparation sold under the name of "Black flag powder." By insufflating this powder about a room, more especially if the doors and windows are closed, the flies are destroyed in a few minutes by asphyxiation, caused probably by the lodgment of fine particles of the powder in the spiracles or tracheæ, thus interfering with respiration. The daily or weekly use of this powder at night in the kitchen and dining-room, where flies are apt to congregate tends to keep the house free from these pests.

Genus Cordylobia (Grünberg, 1903)

This genus presents the following characteristics: Prominent eyes, distinctly separated in the middle in the female and almost touching



FIG. 346.—Cordilobia anthropophaga, female × 4. (*After Castellani and Chalmers.*)

in the male; third segment of antennæ three times larger than the second; body short, almost globular, hairy, and yellowish brown in color; thorax and abdomen marked with longitudinal dark streaks; wings of a brownish tinge. The type of the genus is *C. anthropophaga.*

Cordylobia anthropophaga (Grünberg).—This fly is of a yellowish-brown color, and measures about 9.5 mm. in length. The head is slightly darker than the remainder of the body, due to the presence of black hairs, especially over the proboscis; the thorax is gray in color and marked dorsally by longitudinal dark stripes. The female is distinguished from the male by the fact that in the former the eyes are separated by a frontal stripe. The larva measures 8 to 12 mm. in length, and is composed of twelve segments, of which the first, anterior or cephalic, is small and pointed and provided with two hooklets.

Habitat and Life History.—The adult lives on decomposing matter and the larva in the skin of man and animals (dogs, cats, rats, etc.). The eggs are not deposited on the skin, but in the soil, and when hatched, the larvæ, which are very active, crawl to the host and, penetrating the skin, form a tumor-like swelling in which they complete their development. This occurs in about twelve days, when they drop to the ground and in about thirty-six hours become pupæ. The adult emerges in from nineteen to twenty-five days (Le Dantec).

Pathogenesis.—The larva is the cause of myiasis of the skin. The lesion resembles a small tumor.

Genus Lucilia (Robineau-Desvoidy, 1830)

Thorax and abdomen have a metallic iridescence, either green or blue, very brilliant, but without a velvety reflection; the first posterior marginal cell is often situated anterior to the tip of the wing.

1. **Lucilia cæsar** (Linnæus) is the common "gold-fly." The larva has been found in myiasis of the skin and intestine. This fly has been suspected of transmitting the virus of poliomyelitis.

2. **L. sericata** (Linnæus).—The larva of this fly has been found in wounds and ulcers.

3. **L. regina** (Macy).—The larva of this species has been found in myiasis of the skin.

4. **L. nobilis** (Meigen).—The larva of this fly has been found in the external auditory meatus.

Genus Chrysomyia (Robineau-Desvoidy)

Thorax and abdomen are of a green metallic iridescence, the thorax being more brilliant than the abdomen, and striped with three well-marked gray longitudinal bands. Antennæ are feathery.

Chrysomyia macellaria (Fabricius, 1794). The adult fly (Fig. 347) measures about 9 mm. in length and is bluish green in color; the wings are transparent and the legs are black. The thorax contains the three black longitudinal bands common to the genus.

The larva of this fly is commonly called the "screw-worm." It is white in color and made up of 12 segments, each one being provided with several spicules arranged in two to four rows (2 for the first, 3 for the second, and 4 for the other segments), in a somewhat spiral manner, hence the name "screw-worm." In addition the larva has two maxillary hooklets and is capable of burrowing into the tissue and causing its destruction, even destroying bones.

Habitat and Life History.—This fly is common in the tropical and subtropical regions of North and South America, and has also been

found in China and India. It is seen especially during the warm season of the year. The female ovulates during the warmest hours of the day, on wounds or in the body cavities, where a larva hatches in about one hour. The larva completes its growth beneath the skin, after which it falls to the ground for pupation.

Pathogenesis.—The larva gives rise to myiasis and deep ulceration of the skin and normal body cavities.

Treatment.—This consists in the injection of chloroform water, calomel, or menthol, suspended in olive oil, or the larvæ may be removed by a surgical operation.



FIG. 347.—Chrysomyia (*Cochliomyia*) macellaria, screw worm fly. *A*, adult; *B*, maggot. × 3. (*A, after Castellani and Chalmers; B, after Blanchard.*)

Genus Calliphora (Robineau-Desvoidy, 1830)

To this genus belongs the common "blue-bottle" fly, which is characterized by the metallic brilliant blue of the abdomen; the antennæ are feathery; the wings are gray in color and semitransparent; the fourth longitudinal vein is bent at an obtuse angle in a V-shaped fashion, and the third longitudinal vein is hairy at the base. The type of the genus is *Calliphora vomitoria*. The larvæ of these flies live as saprozoa in decaying organic matter, but may occasionally be found in wounds and in the normal body cavities.

1. **Calliphora vomitoria.**—The larva of this species has been found in the nasal cavities and in the intestine of man.

2. **C. erythrocephala** and **C. azurea** are merely saprozoa.

3. **C. limensis.**—The larva of this fly has been found in cases of myiasis of the nose in Chili.

Genus Auchmeromyia (Schiner, Braur, and Bergenstamm, 1891)

The members of this genus present the following characteristics: Eyes in both sexes are separated by a wide streak; antennæ feathery; body yellowish brown in color, without metallic iridescence; abdomen composed of four segments, the second segment being as large as the other three combined. The type of the genus is represented by *Auchmeromyia luteola*, the larva of which, like the leeches, sucks the blood of man and animals.

Auchmeromyia luteola (Fabricius, 1805).—The *adult fly* is 10 to 12 mm. in length, yellowish in color, and covered with small black



FIG. 348.—*Auchmeromyia luteola*. Congo floor maggot (*B*) and adult female fly (*A*). *A*, × 3; *B*, × 4. (*After Manson in Chandler.*)

hairs, which give it a smoky appearance; the head is prominent and as broad as the thorax; the proboscis is folded beneath the thorax into a groove; palpi are club-shaped, and the eyes are separated by a wide streak; the thorax has two narrow and inconspicuous longitudinal bands; the second abdominal segment is very large; the legs are of the same color as the body, except for the first tarsal segment, which is black.

The larva is called the "Congo floor-maggot." It was found by Dutton, Todd, and Christy in the ground at a depth of three inches. When fully grown it measures up to 17 mm.; it is dirty white in color, acephalous, and composed of eleven segments. The first anterior segment is small and contains the mouth, which is provided with hooks.

The last segment contains the anus and two spiracles. The ventral surface is slightly flat, and on the side each segment contains spines, protuberances, and pits.

The pupa is dark brown or black in color, and measures 9 to 10.5 by 4 to 5 mm. It is marked by annular ridges, and is differentiated into a narrower anterior and a rounder posterior portion.

Habitat and Life History.—This fly is distributed widely in tropical and subtropical Africa. The adult does not bite, as does the larva, which is nocturnal in habit and comes out of the hole to suck the blood of persons sleeping on the ground or on low beds.

The fly lays its eggs on the ground, where a larva hatches and burrows its way below for protection. Coming to the surface at night in search for food, it bites man or animals, after which it again burrows under the ground. This process is repeated at intervals until it is fully grown and becomes a pupa. The pupal stage lasts from two to three weeks, after which the pupa develops into an imago.

Pathogenesis.—The experiments of Dutton, Todd, and Christy failed to show that sleeping sickness was transmitted by the larva. Although a pest, because of its biting habit, the insect is apparently without pathologic importance.

FAMILY ANTHOMYIDÆ

Arista either naked or pectinate; thorax with complete transverse sutures; first posterior cell completely open; abdominal bristles usually absent. The family includes several genera, of which *Anthomyia*, (*Fania*), *Hylemyia*, and *Hydrothea* contain species that are occasionally parasitic on man. They are differentiated by the following characteristics: *Anthomyia* (Meig), arista bare; *Hylemyia*, arista plumose; *Hydrothea*, arista pubescent.

Anthomyia canicularis (Linnæus) (*Fanuia canicularis* of recent authors).—The adult fly bears some resemblance to the house-fly, from which it is easily differentiated by its slender body, which is set with bristles. This fly is commonly found in houses in Europe and North America. The *larva* can easily be recognized by the presence of long appendages in the segments. Like the house-fly, this fly lays its eggs on decomposing organic matter and fermenting vegetables. The larva is commonly saprozoic in habit, but it has been found in man in the feces and in vomited matter. Chevrel found the larva in cases of myiasis of the urinary passages.

Other species of this family are *A. scalaris*, *A. saltitatris*, etc., which have been found in the feces.

Hydrothea meteorica (Robineau-Desvoidy).—This fly is common in stables, and lives on the sweat of horses, mucus from the nostrils, tears, etc. Owing to this peculiar habit, the fly is especially well

adapted to act as a carrier of pathogenic bacteria, which, deposited on the eye, in the nostrils, etc., may cause infection of the part. It may also attack men.

III. PUPIPARA

Family Hippoboscidæ

The following are the characteristics of this family: Body and head flattened; antennæ single jointed, with terminal arista; proboscis well defined and adapted for biting and for sucking blood; wings are well developed, rudimentary, or absent; tarsi are usually provided with claws, which enable the fly to cling to the hair of its host. The family contains the following genera: *Hippobosca* (Linnæus, 1761); *Allobosca speiser; Olfersia; Pseudo-oljersia; Lipotena,* and *Melophagus.* Only a few species are of importance here:

1. **Hippobosca equina** (Linnæus).—This species is parasitic on horses, cattle, dogs, etc. The fly measures about 8 mm. without the wings, and lives by preference on the neck and perineum of the host. Not infrequently it may be seen running upon the hairs of the skin. In the absence of domestic animals, it may attack man.

2. **H. camelina** is found in Africa.

3. **H. rufipes** is believed to transmit *Trypanosoma theileri,* which is the cause of "galziekte" in cattle in South Africa.

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CHAPTER XXV

CLASS INSECTA (Concluded)

ORDER III. SIPHONAPTERA

Wings absent; body laterally compressed; antennæ three-jointed; distinctly separated thoracic joints. The order comprises three families: *Sarcopsyllidæ*, *Pulieidæ*, and *Ceratopsyllidæ*, all of which are important in human parasitology.

FAMILY SARCOPSYLLIDÆ

The following are the characteristics of this family: Mouth parts well developed and adapted for piercing, mandible large and strong; labial palpi not articulated. Thorax generally short, and usually smaller than the first abdominal segment. Wings are absent. The abdomen of the female is capable of considerable distention; legs are very prominent and strongly developed, especially the hind leg, which is usually as long as or longer than the body, and thus enables the insect to jump to a considerable height. Color either a dark yellowish or reddish brown.

The family contains several genera: (1) *Echidnophaga* (Olliff, 1886), characterized by the presence of a patch of spines on the inner side of the hind coxa; (2) *Hectopsylla* (Frauenfeld, 1860) marked by the absence of the patch of spines on the hind coxa; hind femur with large, basal, tooth-like tubercle; (3) *Dermatophilus* (Guérin, 1838), characterized by the absence of the patch and tubercle in the hind coxa and femur respectively (Jordan and Rothschild), etc. Of these three genera, only the genus *Dermatophilus* need be considered here.

Genus Dermatophilus (Guerin, 1838).—As has previously been stated, the characteristics of this genus are the absence of the patch of spines on the inner side of the hind coxa and of the tubercle on the hind femur. Eyes may be present (*D. penetrans*) or rudimentary (*D. cecata*). Color, reddish brown.

1. **Dermatophilus penetrans** (Guerin, 1838).—This insect, variously known as chique, chigre, chigo, "jigger," or "nigua," resembles the common flea of the dog and cat, from which it can be differentiated by its smaller size, measuring only about 1 mm. in length; by the fact that the posterior part of the body is whitish in color and the mouth is provided with a well-developed proboscis, by means of which the insect penetrates the skin (Figs. 349, 350).

Habitat.—The home of this insect is believed to be tropical America, especially Brazil, from which it has been transported to Europe, Africa, and the Orient, as far as India. It is not known to occur in East Asia. It is especially common in the south of Mexico, Central America, and the northern part of South America, where, in some regions, it is a veritable pest. It thrives best in warm, dry, and sandy soil, hence it is more common during the dry season, especially in March and April in tropical America. The larva and the adult male and female live on the soil, feeding occasionally on the blood of man and of animals, especially of hogs. After impregnation, the female penetrates the skin of man or of animals, matures its eggs, and gives rise to itching and irritation, and paves the way for the occurrence of infection and ulceration of the feet, which are the parts most commonly affected in man, crippling the person and occasionally causing deformity or loss of one or more toes, etc.



FIG. 349.



FIG. 350.

FIG. 349.—Dermatophilus (Sarcopsylla) penetrans before feeding. (*After Brumpt.*)
FIG. 350.—Head of Dermatophilus (sarcopsylla). *t*, Proboscis; *pm*, palpes; *md*, mandibles; *mx*, jaws; *af*, antennæ fasset. (*After Brumpt.*)

Life History.—The impregnated female enters the skin and lodges beneath the epidermis, the head being at the bottom of the burrow and the posterior abdominal segment toward the surface, blocking the opening. At this point the insect can be seen on the second or third day, as a tiny whitish speck, which, if extracted, appears almost round, resembling a minute pearl. In about a week's time the female has grown to a large size, measuring 2 to 4 mm. in diameter. This growth is due to the distention of the abdomen with the eggs. As the eggs become fully formed the insect turns brown or almost black in color. In a few days the eggs are discharged through the original opening in the epidermis made by the entrance of the insect, and fall to the ground, where they hatch yielding larvæ, which become pupæ and imagos in from eight to ten days. The female jigger is expelled by ulceration or dries up.

Pathogenesis.—The invasion of the skin by a "jigger" is called *Dermatophiliasis*. The infestation is common among the lower classes and especially among children who go about barefooted, a habit that

is very common in the tropical countries. The presence of a few jiggers, more especially if left undisturbed, rarely gives rise to a more than localised itching and slight irritation. As a rule, in some localities, most persons are attacked by this insect some time during the summer, but no notice is taken of it until the jigger has grown to sufficient size. The itching and irritation, however, may be so marked as to attract the attention, and attempts are made to remove the insect by means of a needle, a thorn, a knife, etc., which are usually unclean, and thus set up bacterial infection.

In neglected cases, especially among children, idiots, and imbeciles, hundreds of jiggers may be counted on a single foot, and as they most frequently lodge between the toes, under the nails, etc., they may give rise to extensive localized lesions, bacterial infection, suppuration, ulceration, and sloughing of the part, with subsequent loss of one or more toes. In some instances tetanus and gangrene may also occur.

Treatment.—Removal of a jigger is best accomplished with a clean needle, after the part has been thoroughly cleaned and disinfected; the operation should be followed by the application of an antiseptic such as tincture of iodin.

Prophylaxis.—This consists in cleanliness about the house, the removal of hogs, poultry, and the like to a point distant from the house, avoiding going about with bare feet, carefully inspecting the feet, especially the toes and the nails, every night before retiring and each morning, and, if present, the removal of the jigger. High boots should be worn, and the floors sprinkled with phenol solution or preferably with petroleum.

2. **D. cecata** (Enderlein) is found in Brazil.

Family Pulicidæ

In this family belong the common fleas, which are usually found as parasites of the lower animals, but which also attack man. In the adult form they are ectoparasites, feed upon blood. As a rule, they have no definite host, since several species may be found on the same kind of animal and, contrawise, several kinds of animals may serve as hosts for the same species of fleas. Since it has been demonstrated that fleas are the chief agents by means of which plague is transmitted from rat to rat, and from rat to man, these insects have recently achieved considerable prominence. Fleas have also been shown to be capable of transmitting *Trypanosoma lewisi* (*Ceratophyllus fasciatus, C. lucifer, Ctenocephalus canis, Pulex brasiliensis*, etc.). They may also serve as intermediate hosts of cestodes, as is the case with *Dipylidium caninum* (*Ctenocephalus canis, Pulex irritans*, etc.).

The chief characteristics of this family are the following: The body is smaller than in Sarcopsyllidæ, and is compressed or elongated;

the head is small in proportion to the remainder of the body; the thorax is wide and well developed; the dorsal surface is round and the ventral surface is covered with hairs; labial palpi are four-jointed; eyes are usually absent; the abdomen is never so greatly distended that the original form is lost; the female is never endoparasitic.

Habitat.—Fleas are distributed widely throughout the world, and are found as ectoparasites of almost all warm-blooded animals, especially mammals. As a rule, they are not permanent parasites. They leave the host for oviposition, the egg usually being deposited upon the soil. When the host is ill, however, the fleas may deposit the eggs on the host. Fleas feed up on blood, and the young insect is said to be capable of living without food for only one to two weeks. The duration of life of a flea is probably about two months. It breeds at all seasons of the year, but thrives best during the summer. Dampness is injurious to the flea, and more especially to the larvæ, which are destroyed or retarded in development by it.

Life History.—The female fleas oviposit on the soil, furniture, carpets, clothes, the nests of birds, etc., or on the parasitized animal when it is ill. The eggs are ovoid in shape, and after several days, depending on the temperature and environments, hatch as vermiform larvæ. These are composed of thirteen segments, set with fine hairs, and provided with a frontal crown in the first anterior segment. The larva feeds on débris and on the excrement of the fleas which abound in the neighborhood; it molts and loses the frontal crown, and the mouth parts appear. It now grows rapidly, then becomes less active, and in about a week spins a cocoon in which pupation takes place. The imago appears after from ten to twelve days, depending on the temperature and surrounding conditions. The young flea now searches for a host, and, finding one, the cycle is repeated.

Pathogenesis.—The bite of the flea produces a small, urticaria-like lesion, which is accompanied by itching, irritation, and redness. In cases in which the bites are very numerous and the skin is tender, a veritable dermatitis may occur, and lead to infection and suppuration.

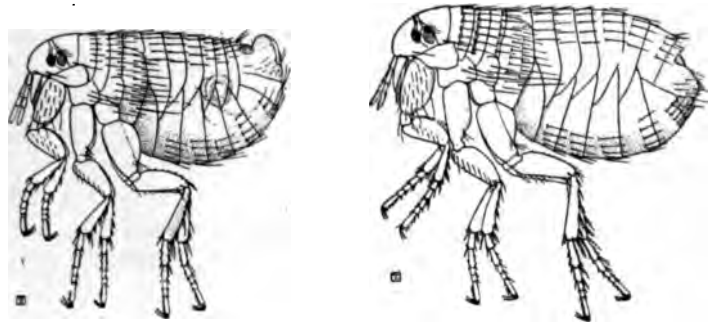
The study of fleas has recently come into considerable prominence as the result of the work of the Indian Plague Commission, as well as that of Simond, Gauthier, Verjbitski, and others, all of whom have shown that these insects are the chief agents in the transmission of plague. It has further been shown that *Bacillus pestis* multiplies in the intestine of the flea. These insects are also capable of transmitting blood parasites, such as *Trypanosoma lewisi*, and serve as the intermediate host of a tape-worm (*Dipylidium caninum*). The following is a list of the fleas that are found on rats and mice, as given by Tiraboschi:

Fleas Found on Mus norvegicus.—*Pulex irritans; Xenopsylla cheopis; Ctenocephalus felis; C. canis; Ceratophyllus fasciatus; C. londiniensis; C. consimilis; C. lagomys; C. mustelæ; C. penicilliger; Neopsylla bidentatiformis.*

Fleas Found on Mus rattus.—*Pulex irritans; Xenopsylla cheopis; Ctenocephalus felis; C. canis; Ceratophyllus fasciatus; C. londiniensis; Ctenopsylla musculi; Dermatophilus cæcata; Echidnophaga rhynchopsylla; E. gallinacea.*

Fleas Found on Mus musculus.—*Ceratophyllus fasciatus; C. londiniensis; C. walkeri; Odontopsyllus charlottensis; Ctenocephalus serraticeps; C. musculi; Typhlopsylla assimilis; T. ogirtes; Hystrichopsylla tripectinata.*

There is no doubt that the foregoing species constitute but a partial list of the fleas that may parasitize rats.



A *B*

FIG. 351.—Pulex irritans. *A*, male; *B*, female.

Fleas That May Attack Man.—According to Brumpt, of the 500 known species of fleas, 'probably 50 per cent. are capable of attacking man. Of these, the following are the most important: *Pulex irritans; Xenopsylla cheopis; Ctenocephalus felis; C. canis; Cerotophyllus fasciatus.*

Fleas That Spread Plague from Rat to Rat.—*Xenopsylla cheopis; Ceratophyllus fasciatus; Ctenopsylla musculi; Ctenocephalus felis; C. canis.*

Fleas That Spread Plague from Rat to Man.—Of the species listed under the head of Fleas That May Attack Man, the most important are: *Ceratophyllus fasciatus,* the most common flea of the gray rat (*Mus norvegicus*); *Xenopsylla cheopis,* which is believed to have as its true host *Mus rattus,* and which is the most common flea that transmits the plague from *Mus rattus* to man.

Classification.—The family *Pulicidæ* is divided into three subfamilies, comprising the following ten genera: *Pulex, Xenopsylla, Ctenocephalus, Odontopsyllus, Pygiopsylla, Ctenopsylla, Stephanocircus, Typhlopsylla, Neopsylla,* and *Typhloceras.* Of these, only

the most important, namely, Pulex, Xenopsylla, Ctenocephalus, and Ceratophyllus, will be considered here.

Genus Pulex (Linnæus, 1758).—Pulicidæ without comb or ctenidia on the head and thorax (Fig. 351); antennal groove closed behind by a genal process; labial palpi four jointed; eyes large; thorax greatly reduced; tergites short and having a row of bristles; coxa pear-shaped, and having spines or hairs posteriorly and at the apex.



FIG. 352.—Pulex irritans larva. *cf*, temporary frontal horn; *d*, antenna. (× 50 *after Brumpt.*)

Pulex irritans (Linnæus, 1758).—This is the only species of the genus *Pulex*. The head is provided with a single hair at the posterior border and another hair anteriorly and below the eye on each side. The *male* measures about 2 mm. in length, and the female from 3 to 4 mm. The body is oval and chestnut brown in color (Fig. 351).

Habitat.—This species is the *P. irritans* of Linnæus, which included all fleas, but is now restricted to the parasitic flea of man. This is an old-world flea introduced into America through commerce. It is found as parasite in badgers, dogs, cats, etc., and especially in man. It is very common in tropical and subtropical America, and in the southern parts of Europe and Africa.

Life History.—The female lays the egg in the ground, where a larva hatches from it and becomes a pupa and adult in from ten to twelve days, depending on the season and the environmental conditions.

Pathogenesis.—This flea attacks man by preference, but also feeds on the blood of animals, such as dogs, cats, etc. The bite is accompanied by irritation and intense pruritus. In some persons the bite may be followed by ecchymosis, surrounded by an edematous area. Bacterial infection and suppuration may ensue. Experimentally this insect has been known to transmit the plague, but under normal conditions this seems to be the exception. It may also serve in the adult stage as an intermediate host for *Dipylidium caninum*.

Genus Xenopsylla (Glinkewicz, 1907).—Pulicidæ without comb or ctenidia; the antennæ three-jointed; eyes round and with three bristles, one in front, one below, and the third near the mouth; palpi four-jointed; posterior coxa have short spines on the inner surface.

Xenopsylla cheopis (Rothschild, 1904).—This species (Figs. 353 and 354) is the common rat flea found in tropical countries all over the

world, and is regarded as the principal transmitter of bubonic plague from rat to man. It resembles *Pulex irritans*, from which it may be differentiated by the presence of a single bristle in front of the eye and another at the oral edge. The fifth segment of the fore- and mid-tarsi has three bristles, ventrally and at the apex.

Habitat.—This flea is believed to inhabit the Nile Valley, and to have been transported with rats all over the world. It lives by preference on rats, but may feed on the blood of other animals and also attack man. It breeds at all seasons of the year, but most rapidly in warm weather.

Life History.—The female lays from one to five eggs, either on the soil or on the host. The eggs are round and almost white in color; in two days they yield a larva that spins a cocoon in about a week. In from one to two weeks the imago escapes from the cocoon, searches for the host, and finding it, the cycle is repeated. The total development, therefore, requires about three weeks.

This flea is regarded as the most important transmitter of bubonic plague from rat to rat and from rat to man.

Genus Ctenocephalus (Kolenati, 1863).—This genus resembles the two varieties just described, from which it is differentiated by the presence of a comb or ctenidium on both the head and the prothorax (Figs. 355, 356). It contains several species that are parasitic on domestic animals, such as dogs, cats, rabbits, etc., and on birds, and that are the transmitters of trypanosomes in these animals. The genus also contains species that serve as intermediate hosts of tape-worms. These fleas are apparently of secondary importance in the transmission of bubonic plague. The common dog-flea, *Ctenocephalus canis*, which is found widely distributed throughout the world is a member of this genus.

1. **Ctenocephalus canis** (Curtis, 1826).—Body brown and more elongated than in the two preceding species. *Male* about 2 mm. and *female* about 3 mm. long. Conspicuous combs of bristles on the prothorax and on the oral ridge, the latter being composed of seven to nine bristles at each side.

Habitat.—This species inhabits by preference the dog and the cat, and occasionally man. It is often found on field-rats and mice. It may live as a permanent parasite on the host.

Life History.—The female lays the eggs on the soil or on the host when ill, and in two days hatches as a larva that feeds on detritus; it undergoes pupation in about one week, and becomes an imago in from six to twelve days, depending on the temperature and the surrounding conditions. When the larva hatches on the animal, it does not feed on the host's blood, but on the excrement of the fleas, which,



FIG. 353.—The Indian rat flea (*Xenopsylla cheopis*, male). × 50. (*After Jordan and Rothschild in Chandler.*)



FIG. 354.—Xenopsylla cheopis, male, schematic drawing; *ab*, abdomen; *th*, thorax; *H*, head. *P*, penis; *cl*, claspers; *st*, stigma; *A*, anus; *Ah*, anal hairs; *Ant*, antenna; *E*, eye; *Oh*, ocular hair; *Orh*, orbital hair; *Mp*, maxillary palpi; *Mx*, maxilla; *Hp*, hip; *Tr*, trochanter; *Fm*, femur; *Ts*, tarsus. (× 22 *after Rothschild N. C. in Brumpt.*)

as a rule, contains blood in a fair stage of preservation, and thus gives the larva its characteristic reddish color.

This flea may serve as the intermediate host to the tape-worm, *Dipylidium caninum*, which is a common parasite of the dog, and which is occasionally found also in the intestine of man.

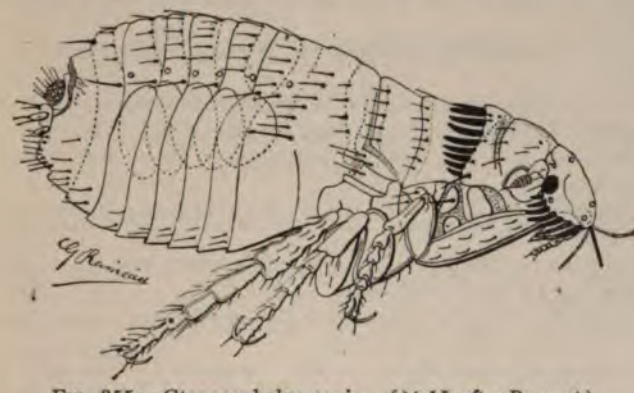


FIG. 355.—Ctenocephalus canis. (× 15 *after Brumpt.*)

FAMILY CERATOPHYLLIDÆ

Genus Ceratophyllus (Curtis, 1826).—This genus resembles Ctenocephalus, from which it may be differentiated by the presence of a ctenidium on the prothorax only. It contains species that are parasitic on rats and mice, dogs, birds, etc., but may occasionally attack man. These fleas are capable of transmitting trypanosomes, tape-worms, and the Bacillus pestis.



FIG. 356.—Head of ceratophyllus. (*After Brumpt.*)

Ceratophyllus fasciatus (Bosc).—This flea is exceedingly cosmopolitan, and is found especially on rats and mice, but is also seen on dogs and birds, but rarely on man. It is one of the intermediate hosts of *Trypanosoma lewisi*, which is commonly found as a parasite in the blood of rats, especially among young animals. It also serves as the intermediate host of *Hymenolepis diminuta* and perhaps of *H. nana*.

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PART IV

VEGETABLE PARASITES

CHAPTER XXVI

GENERAL CONSIDERATION OF VEGETABLE PARASITES

The Fungi.—History.—Morphology and Structure.—Reproduction.—Habitat.—Life History.—Artificial Cultures.—Effect of Environmental Conditions.—The Evolution of Parasitic Fungi.—Mechanism of Transmission.—Pathogenesis.—Classification.

The vegetable kingdom is divided into five groups: I. *Protophyta*, or primitive bacteria; II. *Thallophyta*, or blue-green *algæ* and *fungi;* III. *Bryophyta*, which group includes the Hepaticæ and the mosses; IV. *Pteridophyta*, or fern plants; and V. *Spermatophyta*, or flowering plants. Of these five groups, the only one that contains the vegetable parasites of man are the *Protophyta* and *Thallophyta*.

The Thallophyta.—This group embraces two classes: (1) The *Algæ* and (2) the *Fungi*. All are morphologically, either unicellular or multicellular plants. When made up of many cells, they are commonly arranged in filaments or threads forming a more or less branched *thallus* or *mycelium*, which is not differentiated into root, stem, and leaves. These plants may show a differentiation, but it is only a rudimentary one. The individual cells of any of the parts may be said to be homologous, in so far as each one is potentially capable of reproducing the parent plant. They are further characterized by the absence of true vessels and of woody tissue.

The Algæ are of no interest in human parasitology, but the Fungi contain important species that are pathogenic for man and animals. The *Bacteriaceæ* (*protophyta*) contains the *Bacteria* which are so numerous as to require separate consideration in text-books upon bacteriology, and will therefore not be discussed here.

THE FUNGI

The fungi, commonly known as *molds*, are low forms of plant life in which *chlorophyl* is absent, and they are, therefore, incapable of undergoing *photosynthesis* or the assimilation of inorganic substances

from the air, depending for their nutrition upon such organic matter as they can absorb from the soil, from animal or vegetable tissues, etc.

The study of these plants is known as *mycology*.

History.—The fungi were studied long before bacteriology became a science. Remak, in 1837, discovered the parasite of "*favus*," which was more thoroughly described by Schönlein in 1839, and in 1843 Grüber discovered the fungus that caused "thrush" and also that which produced "ring-worm."

As early as 1848 Langenbeck, in Berlin, pointed out the transmissibility of actinomycosis (lumpy-jaw) in cattle to man; Bollinger, in 1877, discovered the fungus of the disease, *Discomyces bovis* (Harz), and James in 1878 and Ponfick in the following year established the identity of the disease in man and animals.

Mycotic affections of the lower extremities were probably known to ancient Indian writers. In 1712 Kaempfer called attention to an enlargement of the feet in India, and in the early nineteenth century the disease was known in that country as Madura-foot, and was regarded as being tubercular in nature. Ballingall, in 1855, first suggested that the affection was parasitic in nature, and Carter, in 1874, found the disease to be due to a fungus, *Discomyces maduræ*, which was isolated in cultures by Kanthack, Hewlett, Vincent, and others.

Originally this organism was believed to be the cause of mycetoma, but recent investigations on the etiology of the disease have shown that it can be produced also by several species of fungi, such as *Sporothrix, maduræ, Aspergillus nidulans, Actinomyces bovis*, etc. According to Brumpt, at least eight different fungi are capable of causing the disease.

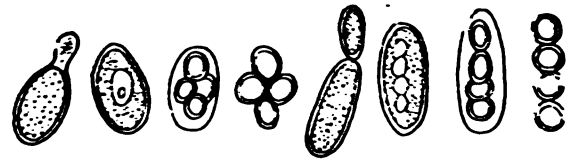
An interesting group of fungi generally known as *Sporotrichæ*, and capable of causing various lesions in man, was discovered by Schenck, in 1898, and later the studies of Hektoen and Perkins, and more recently of Beuermann, Gougerot, Dor, Widal, Sabouraud, and others, have differentiated the lesions from those of scrofula: syphilis, tuberculosis, etc., with which they were formerly confounded.

Certain mycotic affections of the lungs and air-passages are now known to be due to fungi of the genus *Aspergillus*, and Blanchard suggested the term *aspergillosis* as a designation for them. *Aspergillus fumigatus* is probably the most common cause of these affections, but several other fungi may, under certain conditions, produce similar lesions.

In recent years an important group of mycotic affections of the skin and internal organs has been described under the name of *blastomycosis*. Gilchrist, in 1894, first discovered yeast-like bodies in sections taken from scrofuloderma-like eruptions, and Buss, in

the same year, described a case of pyemia due to the saccharomyces (Sp?). The disease has been studied chiefly by Rickets, Ormsby, Hyde, Montgomery, Pusey, and others in America, but the condition seems to be common in the tropics.

Morphology and Structure.—The vegetative system in fungi is commonly represented by a globular or filiform cylindric structure known as the *hypha*, which consists of a membrane inclosing the protoplasm, which develops by apical growth. When young, the hypha is undifferentiated, but as it develops it usually becomes transversely septate, branched, and arranged in characteristic bundles or masses that collectively constitute the *mycelium* or *thallus* (Figs. 358, 366). Exceptions to this mode of structure may, however, occur: thus in yeasts and allied forms, the plants consist of a succession of ellipsoid cells formed by budding; in *Chytridiaceæ* the structure consists of oval or spheroid cells (Fig. 357), whereas in *Protophyta* the simplest forms—bacteria—the prevailing types are minute spheres or rods that multiply by fission.



A *B* *A* *B*

FIG. 357.—Saccharomyces anginæ showing vegetative forms *A* and spore forms (ascospores) *B*. (*After Troisier and Achalme in Brumpt.*)

In addition to the vegetative form of reproduction, fungi commonly reproduce by spore formation, and the spore may be exogenous, and situated either at the end or at the side of the mycelial thread, or endogenous, when it is inside the hypha. The disposition and arrangement of the spores serve as a basis for classification.

The morphology of fungi in general presents such variations that, in describing the group as a whole, no characteristic type can be given. As a rule, however, a fungus consists of three parts: (1) *Hypha;* (2) *thallus* or *mycelium;* and (3) *fruit-body*, or reproductive system.

1. *The Hypha.*—The hypha is the fundamental structural unit of a fungus. It may consist of a single cell, as in yeast, or of a chain of oval cells, as in *Endomyces* (*E. albicans*), being either branched or unbranched.

2. *The Thallus or Mycelium.*—In the simplest form, the thallus may consist merely of several hyphæ, whereas in the higher types, as in those of the family *Mucoridæ* (Rhizomucor), it is differentiated into a root system of mycelia—the *rhizomes;* an aërial portion, or *mycelium proper*, and a reproductive portion, fruit-body, or *sporan-*

gium (Fig. 361). The thallus may be undivided (*Mucor*), septate (*Aspergillus, Trichophyton*, etc.), or divided into dichotomous or lateral branches, forming an entanglement or net-like growth, the branches sometimes interlacing or crossing each other, forming characteristic bodies or masses called *pseudo-parenchyma*.

In mushrooms the interwoven hyphæ form a compound fungus-body of definite and regular shape, which is differentiated into a *mycelial root system*, a *stipe*, or stem, and the *pileus*, or head, which carries the spores in the gill-chambers.

Finally, in certain other fungi, such as *Madurella, Actinomyces, Trichophyton*, etc., the mycelium is very fragile, and under certain conditions may break into "sporoid bodies" that have erroneously been called *mycelial spores* (Fig. 384).

3. *The Reproductive System.*—Most fungi reproduce by spore formation, and the spores may be formed within the mycelium, at its end or at its side, or in specialized bodies known as *sporangia*.

The Sclerotium.—Under unfavorable conditions, or when the growth becomes old, the mycelium of some fungi gives off numerous branches that become entangled and fused into a more or less rounded and compact mass (pseudo-parenchyma), which finally becomes surrounded by a protective membrane and forms a tubercle-like body called the *sclerotium*, which may or may not contain spores. The sclerotium represents the dormant or resting stage of the plant, and when surrounded by favorable conditions of moisture and temperature, may give rise to a new thallus.

Dysmorphism.—This term is applied to the peculiarity possessed by certain fungi of appearing under a variety of forms that differ so from one another, that, were it not for their culture in artificial media, in which they present more or less constant and characteristic manifestations, they would readily be mistaken for a species belonging to a different genus. This dysmorphism becomes more evident when a comparison is made between the growth of the fungus as a parasite and that which takes place as a saprophyte in culture. Thus the characteristic growth of *Actinomyces* in the tissues of an animal (Figs. 379, 380, 381, 382) is that of a mycelial mass made up of a collection of hyphæ arranged in a radiating manner and converging at the center, where mycelial spores are found, whereas in artificial culture (Fig. 384) the growth consists merely of fine, delicate filaments. Similar variations may be observed in *Trichophyton, Microsporon, Blastomyces*, etc.

Nutrition.—Being deprived of chlorophyl, the fungi are incapable of using the carbon dioxid and other inorganic substances from the air, and therefore derive their food material from complex organic compounds, such as the decaying organic substances that are present in the substratum in which they grow. Like bacteria, fungi produce

ferments that act on the raw organic material, digest them, and render them assimilable so that they can be absorbed by the plant.

Growth.—Like bacteria, the fungi grow by elongation, forming long filaments or hyphæ that either remain single or become branched, forming dichotomous or lateral threads.

Reproduction.—Two forms of reproduction take place in fungi, namely, asexual and sexual.

Asexual Reproduction.—The asexual or vegetative constitutes the most common mode of reproduction in fungi, and consists either in the formation of new hyphæ or in the production of spores.

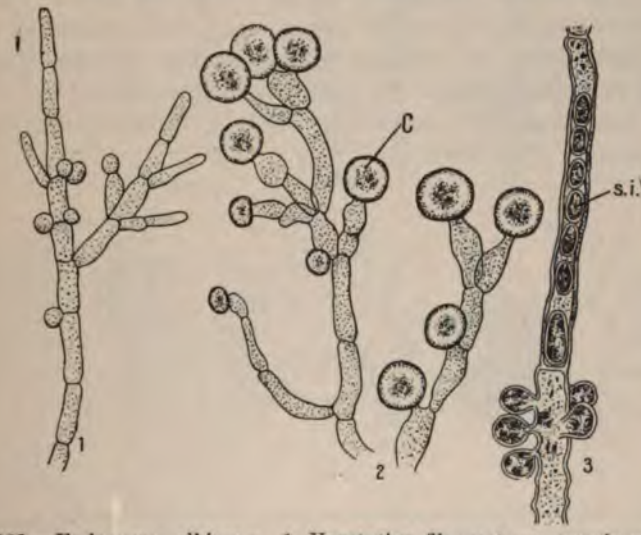


FIG. 358.—Endomyces albicans. 1, Vegetative filaments as seen in preparations from the lesion in the mouth (thrush); 2 and 3, filaments as seen in artificial culture; *c*, terminal chlamydospores; *si*, endogenous and *exs*, exogenous chlamydospores. (*After Vuillemin in Brumpt.*)

The *spores* (Fig. 358) are oval or round bodies, consisting of an outer membrane, or *exposure*, inclosing the cell proper, or *endospore*. The spore may appear outside of the hypha, as an *exospore*, and be situated either at the side of or at the end of the filament, or it may exist inside a special cell as an *endospore*. Not uncommonly these spores are collected into a specialized structure at the end of the hypha, forming the fruit body, or *sporangium*, which consists of a *columella* around which the spores are located, the whole being surrounded by a delicate membrane, the peritheca (Fig. 359). The spores are sometimes arranged in a definite fashion, forming a characteristic pattern. Thus in *Mucor* the fruit-body is globular; in *Aspergillus* it is radial; and in *Penicillium* it is tuft-like, the body consisting of three or four branches that divide dichotomously, each supporting a chain of spores

at the end. Various names have been applied to the spores, depending on the morphology, location, relation to the hypha, grouping, mode of formation, etc. Five asexual types of spores may be recognized.

1. *Conidiospores.*—These are exospores, formed by budding on the hypha. They are situated either at the side or at the end of the filament or *sporophore* (Fig. 360). When terminal, they are not uncommonly numerous and arranged in a chain, as in *Penicillium* and *Aspergillus* (Fig. 359). Such spores may all be of the same size, or some may be large (*macroconidia*) and others small (*Microconidia*).

2. *Basidiospores.*—These are *exposures* formed on the tip of long and slender processes (*sterigmata*) at the end of the hypha (Fig. 360).

3. *Gonidiospores.*—These are *endospores* formed inside of a spore capsule (*sporangium* or *zoösporangium*), usually terminal and aërial (mucord) or intramycelial. In some cases these spores are free and provided with organs of locomotion (cilia or flagella), when they are called *zoöspores* (Fig. 360).

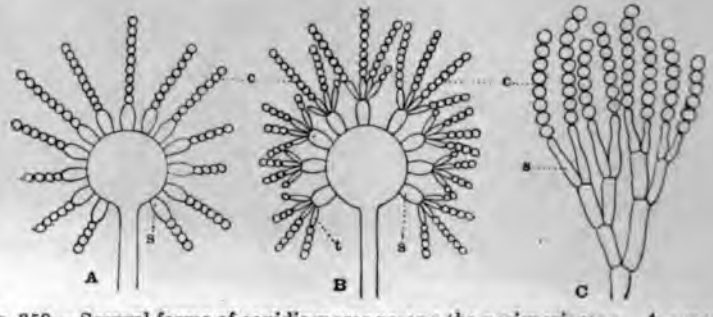


FIG. 359.—Several forms of conidiospores among the perisporiaceas. *A*, aspergillus; *B*, sterigmatocystis (aspergillus); *C*, penicillium; *s* and *t*, primary and secondary sterigma respectively; *c*, conidiospores.

4. *Chlamydospores.*—These *endospores*, also called ***endoconidia***, are provided with a thick membrane. They may be terminal, lateral, or intramycelial.

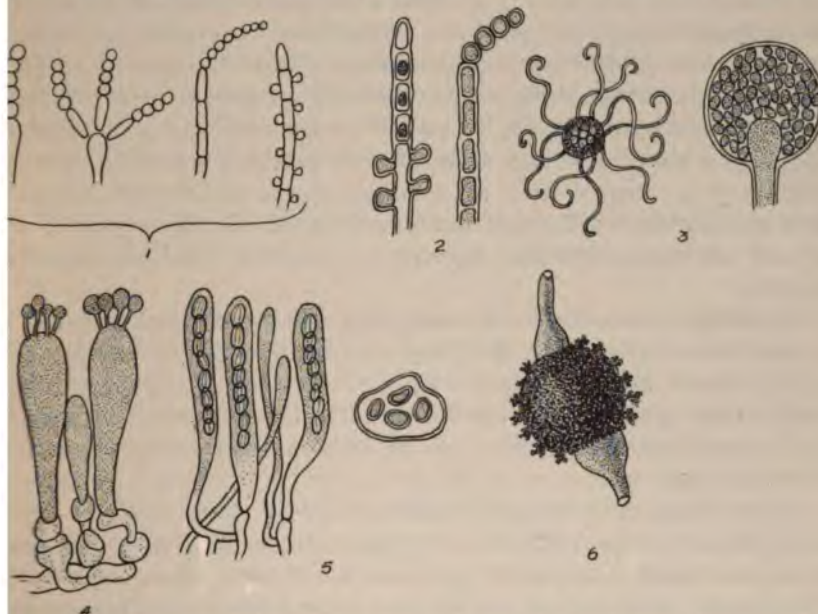
5. *Ascospores.*—These are endospores, four or eight or a multiple of eight in number, arranged in a single line, and formed inside of a special sporangium or *ascus*. The spores have a thick membrane which is divided into two layers (Fig. 360).

As may be seen, this classification of spores does not furnish sharp differentiation, which accounts for the fact that the conidio- basidio- and gonidio-spores are often known only by the last name.

Sexual Reproduction.—Sexual reproduction is very rare among the parasitic fungi of man, being observed only in the *Mucorinæ*. The phenomenon may take place either by the conjugation of two undifferentiated hyphæ or by complete sexual reproduction.

1. *Conjugation.*—This is a form of *isogamy.* Two sexually differ-ıtiated parts of the hyphæ (*gametes*) unite, fuse, and give rise to the ırmation of a new large cell at the point of union. This becomes ırrounded by a double membrane, and forms a *zygospore* (Fig. 360).

2. *Complete Sexual Reproduction.*—This is a process of *heterogamy.* ne of the hyphæ becomes differentiated into the female element, *ısporangium* or *oögonium,* containing one or several protoplasmic ɔdies surrounded by a thick wall pierced by pores—*macrogametes* *oöspheres;* another hypha, much smaller and more delicate than the



G. 360.—Diagram of the different types of spores in fungi; 1, condiospores; 2, chlamydospores; 3, gonidiospores; 4, bacidiospores; 5, ascospores; 6, zygospores.

t, is differentiated into the male element, the *antheridium.* This es in contact with the oösporangium, and sends a protoplasmic cess into it through the pores in the wall of the membrane. In some s the antheridium divides into several motile bodies known as *rogametes, antherozoids,* or *spermatozoids,* which enter the oösporan-n, and is followed by fertilization. In either case the fertilized *porangium* gives rise to a sexual spore known as the *oöspore.*

Of the two modes of reproduction, the asexual form is the most mon and constant in all cases, whereas the sexual variety occurs rarely and seems often to be arrested during the life history of the asitic fungi.

Habitat.—As a rule, fungi are free living plants, and are found ely distributed in nature, growing as saprophytes on decayed or-

ganic matter. Not a few species, however, have become adapted to a parasitic existence and live upon animals and plants.

Life History.—The life history of the fungi is very simple. They are usually saprophytic in nature, and occasionally occur as parasites on man, animals, and plants. Reproduction is commonly asexual, and consists merely in the vegetative growth of the hypha and mycelium and the subsequent production of non-sexual spores (conidiospores, chlamydospores, etc.). In a few instances conjugation or true sexual fertilization may take place, with the formation of sexual spores, as has previously been described. In either case, under favorable conditions, the spore germinates and produces a hypha and a mycelium, and eventually spores and the cycle is repeated. This complete or typical life cycle, however, while easily observed in nature or in artificial cultures, when undergoing a parasitic existence (as in man or in animals), is incomplete and atypical, and consists merely in the production of mycelial threads or of a collection of undifferentiated cells, thus making their differentiation almost impossible; hence the necessity of employing artificial cultures for the study and identification of fungi.

Artificial Cultures.—In few instances the fungi when growing as parasites on the surface of the body or in the normal external cavities, may produce spores (chlamydospores, conidiospores, etc.). This makes their generic classification possible, but, as previously stated, their study and identification can be accomplished only as the result of artificial culture.

Most fungi tend to grow readily on bread, potatoes, beer-wort, fruit-juices, carrots, milk, etc., but since the chemical composition of these substances tends to vary and exerts a decided influence upon the morphology of the growth, the use of standard artificial culture media, temperatures and surrounding conditions is to be recommended.

The media employed may be either liquid or solid.

Liquid Media.—Fungi in general grow well on ordinary bouillon and in dextrose or maltose bouillon.

Solid Media.—Agar or a special medium having plain agar as a base, and containing peptone and saccharose, dextrose, maltose, etc., in the proportion of about 1 to 5 per cent. is satisfactory.

The Medium of Sabouraud.—As a routine, the medium of Sabouraud will be found satisfactory in most cases. Its composition is as follows:

Maltose	4 gm.
Peptone	1 gm.
Agar	1.5 gm.
Distilled water	100 cc.

It should be remembered that media containing a high percentage

of sugar tend to produce vacuolation of the protoplasm, which may be mistaken for spore formation (pseudo-chlamydospores).

Effect of Environmental Conditions.—*Effect of Temperature.*—Temperature has a great influence upon growth. Few parasitic fungi grow well at a temperature of 37° C., whereas the majority thrive best at from 30° to 35° C., or at a room temperature that corresponds to the average temperatures in which the fungi live as ectoparasites on the body. A temperature of 37° C. not merely retards their growth, but is detrimental and should be avoided. As a rule, a temperature of 30° C. will be found most satisfactory.

Effect of Oxygen.—The presence of air is essential for the growth of most fungi, and although some species may grow anaërobically, they are apt, under such conditions, to show dysmorphism, as, for example, in the case of certain *Mucinæ*, in which the hyphæ may show abnormal budding and so may resemble yeast-cells. Only a few fungi are anaërobic.

Effect of Light and Moisture.—These tend to influence the growth of fungi. As a rule, they grow in the dark and with a moderate degree of moisture.

Mode of Examination.—The parasitic fungi may be examined either directly, *i.e.*, as found in the hair, skin, organs, etc., or in culture. The latter method is more satisfactory, and for certain forms, as, for example the *Sporotricha*, cultural methods are indispensable. The material is carefully removed, and bacterial contamination avoided as much as possible; it is then inoculated in an appropriate medium—either on plates or on slanted agar—and incubated at room temperature or at 30–36°C. The first growth is apt to be impure, but the particular fungus can be isolated by subsequent transplantation. Bacterial contamination may be avoided by previously immersing the material in absolute alcohol for a few minutes, which destroys the bacteria, but not the fungus.

In direct examination, a fresh cover-glass preparation is made of the fragment of tissue or material, and examined under the microscope. Spreads should also be made and stained by the Gram method or with diluted fuchsin, borax, methylene-blue, etc. A test for the acid-fast properties, as is done in the case of tubercle bacillus, may also be made with advantage in some cases as some fungi, not uncommonly, exhibit acid-fast properties.

The tissue, hair, plaques, skin, etc., may be cleared by treating the material with 10 to 30 per cent. potassium hydroxid solution—for some hours if cold, or for a few seconds at the boiling temperature; the suspension should then be centrifugalized and the sediment examined.

In studying the lesions the tissue should be embedded in paraffin or celloidin, sectioned, stained, and examined. The same procedure

may also be employed in making an examination [illegible] of portions [illegible] fixed in the [illegible] formalin, embedded in paraffin and sectioned.

The Evolution of Parasitic Fungi.—The life history of the fungi that are of interest in medicine shows clearly that they may properly be regarded as merely occasional or incidental parasites. It will be seen that from the saprophytic existence normal to them they may under certain conditions take up a parasitic life which with few exceptions is not essential to complete their life cycle and may properly be regarded as a simple phenomenon of adaptation to environment. This makes their study so much more important from a practical as well as from a scientific point of view, as the development of pathogenic fungi in the body (*Actinomyces*, *Aspergillus*, *Trichophyton*, etc.) is commonly the result of a traumatism or of physicochemical changes in the part, and it is naturally a question whether these organisms are primarily the cause or the effect of the infection.

Certain parasitic fungi, such as *Trichophyton*, which are [illegible] and in which the parasitic habit appears well established, have undoubtedly had a saprophytic origin, since they can be cultivated artificially (Sabouraud, R. Blanchard). Aspergillosis and blastomycosis are likewise sporadic affections, which show the occasional adaptation to a parasitic life of these fungi (*Aspergillus* or *Saccharomyces*), which are found abundantly in our daily food, liquids, cheese, fruits, or in the air.

A curious fact is that certain fungi, such as *Hemispora* [illegible] [illegible], and *Sporotrichum beurmanni*, are sometimes found in gummatous tumors on the surface or in the normal cavities of the body, especially on the mucous membrane in lesions [illegible] as sporotrichosis. Are not these cases of adaptation of these fungi to what apparently seems to be a parasitic life, but which is in reality merely a saprophytic existence on a preëxisting syphilitic gumma? The fact that iodin and antisyphilitic treatment are regarded as specific in such cases may possibly serve to support this view.

Another curious phenomenon peculiar to mycotic diseases is that similar affections are produced by different species of fungi, and that the lesions produced by these organisms are seldom so characteristic as to permit a clinical diagnosis to be made without the aid of the microscope. This is the case, for example, in favus, mycetoma, actinomycosis, gumma, ulcerations, etc. Furthermore, in these lesions the dysmorphism of the parasite is such that it is often necessary, for its identification, to study the fungus under the normal environment of a saprophytic existence—that is, in artificial culture. All this

undoubtedly points to the fact that in most fungi a parasitic existence is an abnormal and acquired condition.

Mechanism of Transmission.—The transmission of fungi, either of the mycelium, or more especially of the spore, may take place by means of certain ectoparasites, such as fleas, mosquitos, ticks, bedbugs, etc., or by natural means, as through the air, infected water, food in a state of putrefaction, etc. As is the case in most parasitic diseases, however, for the growth and multiplication of the parasites in the new environment it is essential that the part parasitized present environmental conditions favorable to the life of the fungi. Thus traumatism, wounds, abrasions of the skin, ulceration, morbid lesions, such as gumma, tuberculosis, certain constitutional disorders, as, for example, diabetes, etc., are important and essential predisposing factors to the development of the infection.

Certain fungi, such as *Trichophyton*, are usually seen only in children, and may disappear spontaneously at puberty; others are more common during adolescence. Tuberculosis is said to predispose to the development of *pityriasis versicolor*, scrofula to *mycetoma*, and an acid sweat to prevent this infection, and an acidity of the mouth is believed to predispose to the occurrence of "thrush." Diabetic persons are known to be subject to fungoid diseases, etc. From what has been said it is clear that this association is not due to a sensitization of the body nor to a symbiotic phenomenon, but merely to the development of changes in the condition of the soil determined by several physicochemical phenomena of which little is known, but which can be compared to the same factors that determine the spontaneous appearance of several species of fungi in nature at certain seasons of the year and under peculiar environmental conditions.

Pathogenesis.—Most fungi are merely saprophytes, but under certain conditions, as has been stated, they may be found as parasites in the body of man, in which they produce a morbid condition generally known as *mycosis*. Although fungi can properly be regarded as *facultative parasites*, they may, nevertheless, give rise to important diseases, such as actinomycosis, blastomycosis, sporotrichosis, mycetoma, etc. The name *ectophytes* has been applied to those parasitic fungi that live on the surface of the body, in contradistinction to *endophytes*, which are fungi living in the normal body cavities or in the internal organs. The lesions produced are due chiefly to mechanical action, and although certain authors believe that a toxic substance is elaborated by some fungi, this has not been satisfactorily demonstrated.

The term *mycosis* was introduced by Virchow in 1856 to indicate all affections produced by fungi, prefixes being added to designate the part affected; thus, *dermatomycosis* (skin); *otomycosis* (ear); *onychomycosis* (nails), etc. Designations that indicate the infecting

species are the terms *blastomycosis* and *actinomycosis; mucormycosis* is also commonly used, and *aspergillosis, sporotrichosis, aspergillosis pulmonæ, actinomycosis cutanea*, etc., are all employed and indicate the type of infection or the part affected.

Classification.—According to the character of the thallus or hypha, and the variety and morphology of the spore produced, the fungi, excluding the bacteria (Schizomycetes), may be divided into five orders: I. Myxomycetes; II. Phycomycetes; III. Ascomycetes; IV. Hyphomycetes; V. Basidiomycetes. Of these, the Phycomycetes, Ascomycetes, and Hyphomycetes are the most important, since they comprise practically all the parasitic fungi of man. The Basidiomycetes embrace only one species of importance, *Ustilago hypodytes*, which is said to be the cause of a peculiar affection known as "friente," or "frien disease," which is common among wood-choppers and field workers. According to some observers, however, this disease is not due to the spores of *Ustilago*, but to an insect, *Aclerda berlesei*, which often swarms in canes. The fluid excreted by the insect is irritating and produces an erythematous dermatitis. The Myxomycetes do not contain species that are parasitic to man.

Order I. Myxomycetes.—These fungi are characterized by the presence of a naked thallus or protoplast, having, as a rule, an ameboid appearance. Reproduction occurs by the formation of spores.

Order II. Phycomycetes.—The thallus is provided with a membrane; hyphæ are white or dark and non-segmented, except at the point of formation of the organs of reproduction; the spore-bearing hypha is usually erect and gives rise to asexual spores and to zygospores. This order takes its name from the genus *Phycomyces*, and includes the families *Mucoraceæ, Peronosporaceæ Saprolegniaceæ* and *Chytridiaceæ*. They are chiefly parasites on plants and animals, and only the Mucoraceæ contain species that are parasitic on man.

Order III. Ascomycetes.—These fungi are characterized by the formation of certain spores termed *ascospores*, numbering 2, 4, 8, or a multiple of 8, inside of special upright cells known as *asci*. The order is dysmorphic, and presents marked morphologic variations depending on the environment. Thus, when parasitic, no asci are found, and reproduction takes place by budding and by means of "*Sporoides*," conidia(?). The order embraces the families *Saccharomycetæ, Gymnoascaceæ* and *Perisporiaceæ*, among which are found species that are parasitic on man.

Order IV. Hyphomycetes.—This order comprises a great variety of fungi, the botanical position of which is not definitely known. In general it may be said that they are characterized by the presence of a septate filamentous hypha, usually delicate, and which, under parasitic existence, may appear as short, slender threads or of bacteria-like

forms. Reproduction takes place by budding and by means of conidia, or perhaps also by means of "sporoids." These bodies are minute, coccoid-like forms found in the hypha or in the meshes of the mycelium. Not uncommonly they are acid-fast, resembling the acid-fast grains found in the lesions of tuberculosis and in *B. leprœ*, etc. These bodies withstand a higher temperature than do the hyphæ.

The morphology of Hyphomycetes varies so widely according to environmental conditions, and the life history of some of them is so imperfectly known that the term "Fungi imperfecti" has been suggested as a designation for the group. It is probable that when this group is better known it will be found to include the *Bacillus tuberculosis*, *Bacillus leprœ*, and allied species.

The order contains several genera, such as *Discomyces*, *Madurella*, *Indiella*, *Trichothecium*, *Monilia*, *Microsporoides*, *Pityrosporum*, *Sporotrichum*, *Trichosporum*, *Hemispora*, *Malassezia*, *Foxia*, etc., which include species parasitic on man. The most important of these will be considered in the next chapter.

Order V. Basidiomycetes.—The hypha is segmented, and reproduction takes place only asexually by means of basidiospores. This order is of no importance in human parasitology.

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CHAPTER XXVII

THE PARASITIC FUNGI OF MAN

ORDER PHYCOMYCETES

FAMILY MUCORACEÆ

The characteristics of the family mucoraceæ are as follows: Thallus not segmented and ramified, the branches being lateral or dichotomous. Some species, such as *Mucor mucedo*, are differentiated into an absorptive system (rhizoids), a vegetative aërial portion (mycelium), and many upright reproductive branches called sporangiophores, each of which ends in a sporangium that contains the spores. Reproduction is asexual and sexual. Sexual reproduction takes place by conjugation, with the formation of *zygospores*, whereas asexual reproduction gives rise to *gonidiospores* or *chlamydospores*. The fungi grow readily in ordinary culture-media at 35° C. in the presence of oxygen.

The family is widely distributed in nature, where the fungi grow on decayed organic substances; some species are, however, found as occasional parasites on man. The genera *Mucor*, *Lichtheimia*, *Rhizomucor*, and *Rhizopus* contain species that are parasitic in man.

Genus Mucor (Micheli, 1729)

Columella present in the sporangium, which is terminal and globular or pyriform in shape; under parasitic conditions the hyphæ form only conidia or chlamydospores.

1. **Mucor mucedo** (Linnæus, 1764).—The hyphæ carrying the sporangia (sporangiophores) are long and erect; sporangium is globular, and measures 100 to 200μ in diameter, it is yellowish in color; spores are elliptic, measuring 6 to 12 by 3 to 6μ; zygospores are spheric, dark, and covered with a thick membrane, measuring 90 to 250μ. Chlamydospores are not produced.

Culture.—This species is found widely scattered in nature and grows very readily on horse dung, from which it can easily be isolated by transplantation to ordinary media or maltose agar.

Pathogenesis.—The fungus produces a fatal disease in bees, and has twice been found as a parasite in man in cases of mycosis.

2. **M. pusillus** (Lindt, 1886).—This resembles the preceding species, from which it is differentiated by the size of the sporangium, which is smaller (50 to 80μ), and the sporangiophore which is shorter.

The columella is claviform. The spores are spheric and smaller (3 to 3.5 μ). It is commonly seen growing on bread, is pathogenic for rabbits, and has occasionally been found in cases of otomycosis in man.

GENUS LICHTHEIMIA (Vuillemin, 1904)

Mycelium is not segmented, and with or without rhizoids; end of sporangiophore terminates in a special expansion for the support of the columella.

Lichtheimia corymbifera (Cohn, 1884).—Mycelium is white; hypha not erect, but lies horizontally on the medium; sporangium

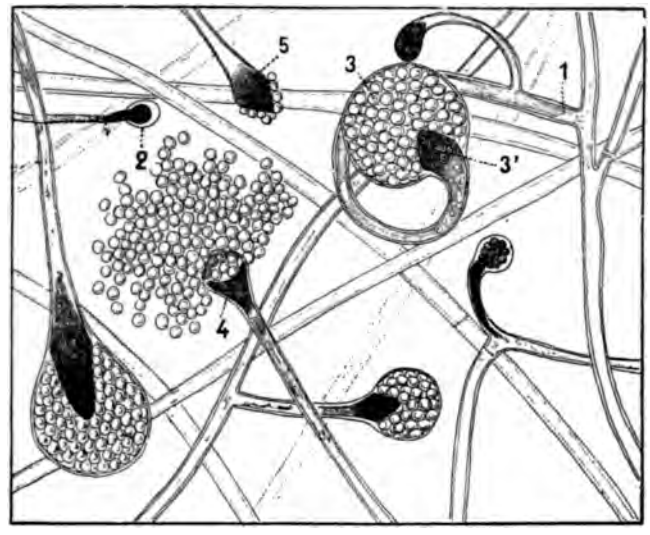


FIG. 361.—Lichtheimia (Mucor) corymbifera. 1, sporangiophore hyphæ bearing two sporangi, one young and the other mature; 2, young sporangium; 3, matured sporangium; 3', columella; 4, columella bearing the spores at the time of dehiscence; 5, columella after dehiscence. (× 440 *after Brumpt.*)

is pyriform (15 to 70 μ); columella is semispheric (10 to 20μ); spores are ovoid (2 to 5 × 3 to 6μ) (Fig. 361).

Cultures.—This fungus grows well on bread, potatoes, etc., and especially on the culture-medium of Sabouraud.

Pathogenesis.—The fungus is pathogenic for rabbits, in which intravenous injection may produce death in from twenty-four to forty-eight hours. It has often been found in man in cases of mycosis of the lung, ear, pharynx, etc.

GENUS RHIZOMUCOR (Lucet and Constantin, 1900)

Mycelium with rhizoids; columella ovoid.

1. **Rhizomucor parasiticus** (Lucet and Constantin, 1900).—Mycelium is grayish when young and brownish later, when it meas-

sures 1 to 2 cm. in length. Sporangiophore is often provided with side rhizoids, and the sporangium is globular (35 to 80μ). Columella is ovoid or pyriform; spores ovoid, 4 by 2.5μ.

Culture.—This fungus grows well on ordinary media, and especially on maltose or dextrose agar.

Pathogenesis.—The fungus is pathogenic for rabbits, and was found once in mycosis of the lung.

2. **R. septatus.**—Found once in man in a case of mycosis of the ear.

Genus Rhizopus (Ehrenberg, 1820)

Mycelium with rhizoids; columella hemispheric and shaped like a mushroom.

Rhizopus niger (nigricans) (Ciaglinski and Hewelke, 1893).—Sporangium black when ripe, and globular in shape. Columella first globular, then cylindric and umbrella-shaped. Spores oval and smooth.

Pathogenesis.—This fungus is found in nature living on decayed organic matter, and may also be found in man in mycosis of the nose, ear, tongue, and lungs.

ORDER ASCOMYCETES

FAMILY SACCHAROMYCETES

The characteristics of this family are as follows: Plant is usually unicellular, round or oval in shape, presenting a wall of single or double contour, containing a granular protoplasm, few vacuoles, and ascospores. Under certain conditions, however, the cell elongates to form mycelial hyphæ and a segmented mycelium, more especially when growing on liquid media, such as fluid beer-wort. Under such conditions it may give rise to side-buds, which separate into conidia, while under unfavorable conditions of food, and in the absence of oxygen, it may develop ascospores. The family comprises the genera *Endomyces*, *Saccharomyces*, and *Cryptococcus*, which contain species that are parasitic on man.

Genus Endomyces (Rees, 1870)

Mycelium segmented. Reproduction takes place by external mycelial spores, chlamydospores (lateral, terminal, or internal), and ascospores.

1. **Endomyces albicans** (Robin, 1853).—The morphology of this fungus varies according to the environment. Two types, the parasitic and the saprophytic, are to be recognized.

The parasitic type, as found in the white patches of the mouth in the affection known as "*thrush*," (Fig. 358) shows a septate mycelial

filament, simple or ramified, measuring 3 to 5 mm. by 50 to 600μ; each cell measures about 20 by 3 to 5μ. At the end or at the side of the mycelium round bodies may be seen which reproduce by budding or by germination when detached.

In artificial cultures the fungus shows a filamentous mycelium, simple or ramified, and also a globular form resembling yeast, which reproduces by budding. Reproduction occurs by chlamydospores or ascospores, and also by internal spores arranged in a single string within the mycelium (Fig. 358).

Cultures.—The fungus is readily cultivated in solid media, where it produces a creamy mass which is irregular in outline and slightly elevated. Development takes place best under aërobic conditions and in slightly acid or neutral media. The organism does not grow on alkaline media.

Pathogenesis.—This fungus is the cause of a well-known mycosis of the mouth known as *thrush*, often seen in children and idiots and cachectic persons, especially in tropical countries. The affection is generally localized, and appears in the form of white patches which are irregular in outline, variable in size, and easily detached. It is generally localized, but may spread to the pharynx, esophagus, stomach, and intestines, or to the larynx and lungs. At times it gives rise to general infection and pseudotuberculosis. It is inoculable into rabbits.

Treatment.—An antiseptic and alkaline lotion, such as sodium bicarbonate, is very efficient in the treatment of thrush. Sweets should be avoided, as they are apt to ferment in the mouth and produce acidity, which favors the growth of the fungus.

2. **E. subtilis** (Blanchard 1895) was found in a pustular eruption. It resembles *E. albicans*, except that the mycelium is more delicate.

3. **E. rhoi** (Castellani, 1909).—This was found in cases of otomycosis.

Genus Saccharomyces (Meyer, 1838)

The fungi belonging to this genus never appear in a filamentous form, but occur as single, round or oval, cells, which reproduce by budding, endospores, or ascospores. These fungi and those of the genus *Cryptococcus* are commonly called *Blastomyces*, and are the cause of a number of well-known mycotic affections of the skin and internal organs, known collectively as *blastomycosis* (Fig. 362). The organism grows readily on culture-media.

These fungi have been found not uncommonly in tumors, and some authors (Sanfelice, Roncali, etc.) regard them as the cause of cancer. The lesions produced by them are so dysmorphic that no characteristic types can be described. They have often been mistaken for syphilis, tuberculosis, tumors, and the like. The affection

is commonly localized, but it may become general, and the diagnosis cannot be made with certainty without the aid of the microscope. The following are some of the species that have been found as parasites of man.

1. **Saccharomyces blanchardi** (Guiart, 1906).—Found in a suspected case of tuberculous peritonitis. The fungus was found in a gelatinous mass weighing about two pounds.

2. **S. anginæ** (Vuillemin, 1901).—Found in a case of tonsillitis (Fig. 357).

3. **S. tumefaciens** (Busse, 1897).—Found in a tumor, etc.

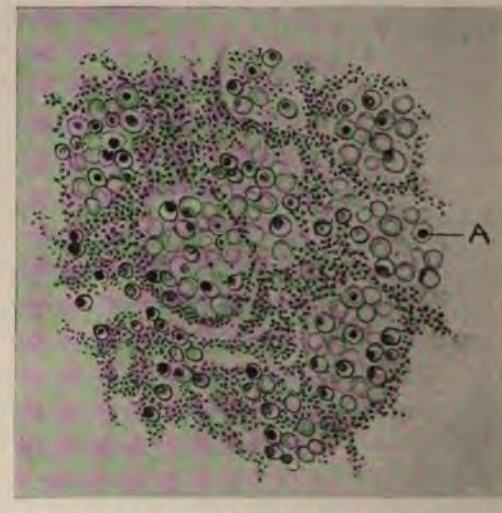


FIG. 362.—Blastomycosis of the lung showing the fungi, yeast-like bodies, *A* in the alveoli.

GENUS CRYPTOCOCCUS

Reproduction occurs only by budding, and ascospores are unknown. The fungi do not ferment the sugars (glucose and saccharose). The parasitic species of this genus may also cause *blastomycosis* in man and animals.

1. **Cryptococcus degenerans** (Roncali, 1896).—Found in sarcomata and carcinomata.

2. **C. hominis** (Vuillemin).—Found in abscesses.

3. **C. gilchristi** (Vuillemin).—Found in ulcerative dermatitis.

FAMILY GYMNOASCEÆ

This family derives its name from the character of the reproductive organs, which are in the form of naked asci. The fruit-body or

sporangium is a small, spheric mass, the wall of which (*perithecium*) is made up of mycelial filaments, which are sometimes differentiated, but do not form a true membrane. From these mycelial threads in the perithecium ascospores, usually lateral and eight in number, are formed. Along with this ascospore formation the majority of the Gymnoasceæ parasitic on man reproduce also by means of conidia or chlamydospores, without the formation of asci, this mode of reproduction is so typical that it may be taken as characteristic of the group, and serves as an important point in identification of the species. The family comprises the genera *Microsporon*, *Trichophyton*, *Epider-*



FIG. 363.—Blastomycosis of the kidney.

mophyton, *Endodermophyton*, and *Achorion*, among which are found species that are parasitic on man. Of these, the following are the most important:

GENUS MICROSPORON (Gruby, 1843)

These fungi are commonly found as parasites in the hair of man and animals. Mycelial spores are round (2 to 3μ). They grow readily on artificial culture-media. Several species are known to affect man and animals, among them being *M. lanosum*, *M. felineum*, *M. caninum*, *M. audouini*, etc. Of these, *M. audouini* is the best known.

Microsporon audouini (Gruby, 1843).—This fungus (Fig. 364), as found parasitic in the hair, appears in the form of a white sheath at the base of the hair. Under the microscope (Fig. 366) it is seen to consist of numerous small spores, 2 to 3μ in diameter, often polyhedral, due to reciprocal pressure, and provided with a double wall. If the hair is cleaned in a 40 per cent. potassium hydroxid solution, it will be seen that the spores are on the outside of the hair, and that they do not invade the medulla, which contains only the mycelium of the fungus. These mycelial threads run parallel to the axis of the hair, and in their ramifications give off short branches, which are terminal or lateral, toward the surface of the hair, and on which they develop spores, forming a peripheral sheath.



FIG. 364.—Microsporon lanosum (audouni). *A*, mycelial filaments in the anterior and *B* and *C*, spores in the cortical portion of the hair; *D*, mycelial fringe of d'Adamson; *e*, epithelial cells. (*After Sabouraud in Brumpt.*)

Culture.—The fungus is easily grown in the ordinary culture-media. The growth is slow, and is visible after the first week, when it appears in the form of white plaques. In a few days aërial branches are given off, complete development occurring in about the sixth week. At this time the fungus often appears as a roundish, central knob, surrounded by concentric rings (Fig. 365). When viewed under the microscope, the fungus presents a dysmorphic growth, which consists of a mycelium containing lateral and terminal conidia, unilocular or multilocular spindle conidia (30 to 60 by 15 to 18μ), and chlamydospores.

Habitat and Mechanism of Transmission.—The normal saprophytic type of the fungus in nature

has not been demonstrated. The transmission is either direct, by contact from animal with man and from man with man, or indirect, as by means of toilet articles, combs, brushes, etc.

Pathogenesis.—Microsporon audouini is the cause of the most obstinate form of Tinea capitis (ring-worm). The disease is common in England and France, but rare in Italy, and is seldom seen in the tropics.

Treatment of Tinea Capit s.—A single exposure of the affected part to the *x*-ray, followed by cleansing with soap and warm water; the application locally of tincture of iodin, 1:10 in 80 per cent. alcohol, and sulphur or mercury ointment, daily, have given beneficial and rapid results in France.

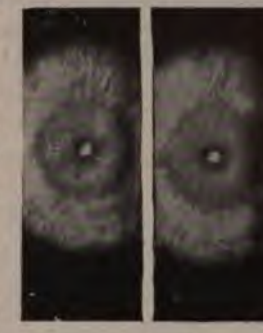


FIG. 365.—Miscrosporon audouini. Culture in maltose agar, 18 days old. Natural size. (*After Sabouraud in Brumpt.*)

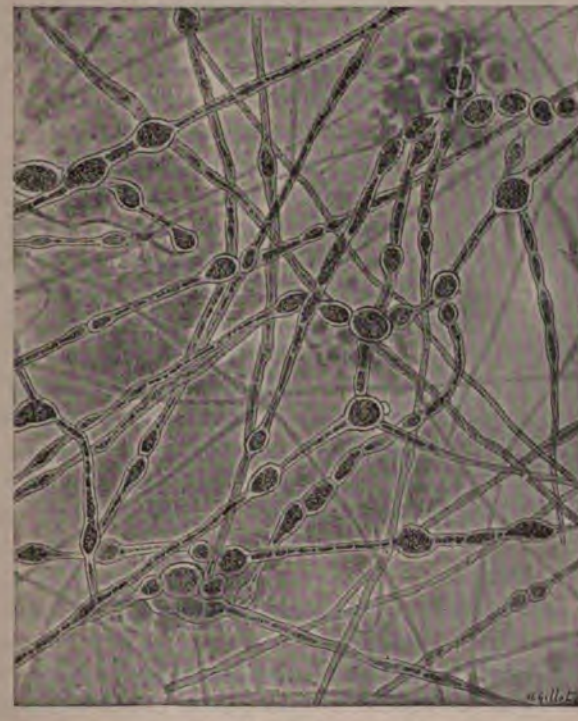


FIG. 366.—*Microsporon audouini.* Artificial culture showing mycelium and chlamydospores. (*After Sabouraud in Brumpt.*)

GENUS TRICHOPHYTON

The mycelial spores are similar to the Microsporon, from which they may be differentiated by their larger size (4 to 7μ). Hairy and

non-hairy parts of the body may be affected by this fungus. Reproduction in cultures takes place by means of terminal or lateral conidia, chlamydospores, and spindle conidia.

Morphology.—In their parasitic existence, the species of the genus *Trichophyton* appear in the form of mycelial filaments and mycelial spores.

The mycelial filaments are found more commonly on the skin than in the hair. They are long, usually cylindric cells, separated by septa.

The mycelial spores are not true spores, but are merely modifications of the mycelial filaments, in which the septa are so close to one another that the individual cells appear to be very short and oval or almost round in shape. These segments, which are very fragile, may break, and when free, they closely resemble spores. The mycelial spores, therefore, being merely the individual cells of the mycelium, are not special organs of reproduction, but simply segments of the vegetative mycelium.

According to the character of the mycelium, two forms of mycelial spores may be found: (1) Oval or roundish, when derived from a "fragile mycelium"—that is, from a mycelium that is moniliform in appearance and that breaks easily; this type is seen in *Trichophyton sabouraudi;* (2) square, when derived from a "resistant mycelium," consisting of relatively long segments or hyphæ. This type is seen in *T. tonsurans.*

According to their location in the hair, the fungi are named—(1) *Endothritic,* when the parasite lives in the interior of the hair, as *e.g., Trichophyton tonsurans, T. sabouraudi, T. violaceum,* etc. These are of human origin, and are transmitted from man to man. (2) *Endoectothritic,* when found on the surface and also inside of the hair, as, *e.g., T. metagraphyte, T. depilans, T. equinum, T. felineum, T. megnini, T. verrucosum, T. ochraceum, T. album;* these are of animal origin, and are transmitted from animals to man. Certain species are found that do not attack the hair; these are known as *tropical trichophyta,* examples being *T. blanchardi, T. ceylonense,* etc., which are common in the tropics.

Laboratory Diagnosis.—For the examination of the suspected material the hair should be carefully removed, so as to extract as much of the root as possible. It should now be placed on a slide containing a few drops of a 30 to 40 per cent. potassium hydroxid solution, and a cover-glass applied. Examine first under the lower power of the microscope, for the selection of a proper field, and then under the high power, for identification. If desired, the preparation may be boiled for a few seconds by passing the slide rapidly over a flame. The infected hair shows the mycelium or "mycelial spore" threads arranged parallel inside and along the axis of the hair, with the spores on the

outside. According to the location of the fungi in the hair, a tentative diagnosis may be made as to whether it is an *endothritic* or *ecto-endothritic* fungus, but both types may show such a resemblance to each other, that it is safer in making the diagnosis, to study the cultural characteristics of the parasite.

Cultures.—Most of the fungi belonging to this genus grow on ordinary solid media or on maltose or dextrose agar. The material may be plated, or merely placed on the surface of a slanted agar tube and incubated at about 30–36° C. The tube should not be closed with a rubber cap nor the cotton plug embedded in paraffin or vaselin, etc., which prevents the free access of air. The growth is often slow, days or even weeks going by before it becomes visible; it is usually impure, and requires subsequent transplantation for isolation in pure cultures.



FIG. 367.—*Trichophyton tonsurans.* Infected hair showing the mycelial filaments made of quadrangular segments. (× 260 *after Sabouraud in Brumpt.*)

Dysmorphism.—Dysmorphism in *Trichophyton* is of common occurrence, and may give rise to such a variation of form as often to render the identification of the species difficult. It is more frequent in old cultures than in young; in those growing at a constant high temperature; or when the aëration of the culture or the amount of moisture in the medium is insufficient. According to Sabouraud, the presence or absence of carbohydrates in the medium also exerts a great influence on the growth, dysmorphism being more common in media containing sugars; and for this reason, therefore, he recommends the use of plain agar.

Animal Inoculation.—The *Trichophyta* are inoculable into susceptible animals, in which they reproduce trichophytosis. The infecting material may be inoculated under the epidermis or the skin. Citron obtained pseudo-tuberculosis of the peritoneum by the inoculation in this region of cultures of *Trichophyton.*

Mechanism of Transmission.—The transmission of *Trichophyton* is usually direct from man to man or from animals to man, or indirectly through the medium of toilet articles, such as combs, brushes, etc. In addition, the artificial saprophytic existence of these fungi suggests

their possible transmission through abrasions of the skin as the result of contact with cultures of the fungus.

1. **Trichophyton tonsurans** (Malmsten, 1845).—This fungus is the cause of the so-called "black-dotted" ring-worm common in tropical countries. The parasite commonly produces a characteristic type of *tinea capitis*, but may also affect portions of the body other than the scalp. Under the microscope the fungus is seen to be endothritic—that is, to grow inside of the hair, where it appears in the form of long filaments made of mycelial spores, quadrangular in shape, and measuring 4 to 5μ (Fig. 367).



FIG. 368.—*Trichophyton tonsurans.* Culture in maltose agar, 20 days old. (*After Sabouraud in Brumpt.*)

Culture.—The fungus grows well on maltose agar and on other media. The colonies are crateriform, presenting a velvety surface when young and a powdery surface when old; white or yellowish in color (Fig. 368).

2. **Trichophyton sabouraudi** (Blanchard, 1897).—This fungus is of the endothritic type, and resembles *T. tonsurans*, from which it is differentiated by the mycelial spores, which are oval or round and smaller. The particles are easily broken off. The fungus is the cause of a form of tinea capitis to which Sabouraud has given the name of "tondante peladoide." It may also cause tinea circinata, onychomycosis, etc.

3. **Trichophyton metagraphyte** (Robin, 1853).—This fungus is of the endo-ectothritic type, the mycelial spores being chiefly on the outside of the hair, and measuring 1 to 12μ (Fig. 370). It is a parasite of animal origin, found in the horse, cow, dog, etc., but is transmissible to man, in whom it usually causes suppuration, and gives rise to a form of trichophytic sycosis of the beard. The fungus grows in maltose agar, where it produces a white excrescence, with elevated center and filaments radiating toward the periphery, which is very characteristic of the type. Other species affecting man are

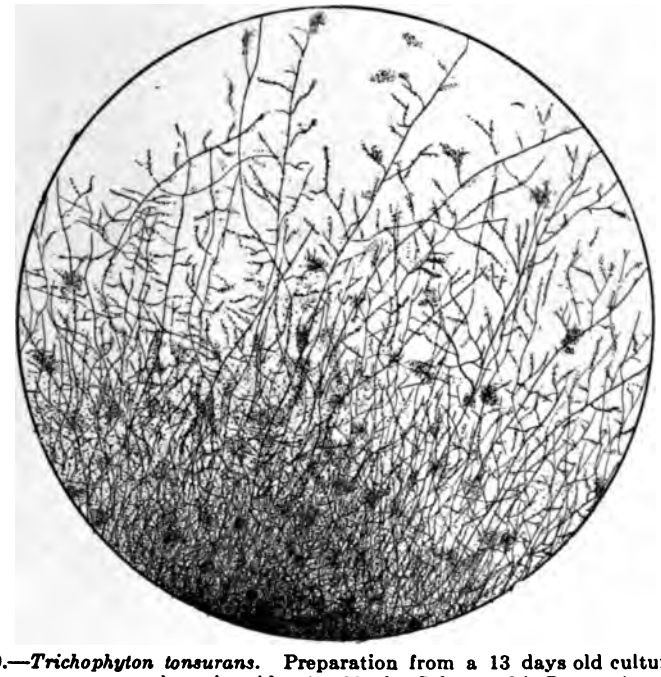


FIG. 369.—*Trichophyton tonsurans.* Preparation from a 13 days old culture fixed in concentrated acetic acid. (× 60 *after Sabouraud in Brumpt.*)

4. **T. violaceum** (Bodin, 1902).—This fungus is found in tinea barbæ. It is endothritic in type. Colonies on agar are brownish when young, and later become violet.

5. **T. flavum** (Fox, 1908).—This fungus is of the endothritic type; colonies with central radial nodule that in time becomes crateriform, etc.

GENUS EPIDERMOPHYTON (Sabouraud, 1907)

The species of this genus were regarded as the cause of *eczema marginatum* in man (Hebra) and according to some authors, also of psoriasis. It is characteristic of them that they affect the skin and

not the hair. In culture they undergo rapid degenerative changes, and do not show conidia, but only conidial spindles.

1. **Epidermophyton cruris** (Castellani, 1905).—This organism is the cause of tinea cruris or "dhobie itch." As a rule, these fungi do not produce suppuration.



FIG. 370.—*Trichophyton metagraphyte* showing the mycelium inside and the outside of the hair. (× 260 *after Sabouraud in Brumpt.*)

Other species found in man are **E. rubrum, E. perneti,** etc.

GENUS ENDODERMOPHYTON (Castellani, 1909)

These fungi, like those of the preceding genus, also affect the epidermis and not the hair. They form a mycelial growth that dissec

the horny layer from the reta malpighii of the epidermis, without giving rise to suppuration.

1. **Endodermophyton concentricum** (Blanchard, 1901) is the cause of tinea imbricata. The fungus is found in the scales. The mycelial threads are 3 to 4μ in breadth and the spores 4 to 5μ.



A *B*

FIG. 371.—*Favus, Achorion schönleinii*. Infected hair showing the characteristic air bubbles after treatment with a 40 per cent. caustic potash. *A*, × 206; *B*, × 75. (*After Sabouraud in Brumpt.*)

2. **E. castellani** (Perry, 1907) is the cause of a dermatomycosis that is common in the tropics, and is known as tinea intersecta. It resembles the foregoing species, with which it is probably identical.

GENUS ACHORION (Lebert, 1845)

This genus probably derived its name from the apparent absence, when stained, of a membrane in the mycelium, or from the germinative

or vegetative nature of the fungus. These organisms are the cau
of the common affection of the scalp and body known as *favus* (F
371), which manifests itself in the for
of yellowish, disc-shaped crusts terme
scutula, which emit an offensive odo
It affects man and animals. In th
parasitic existence the segments of th
mycelium are much longer than in th
genus *Trichophyton* or *Microsporo*
Grown on solid media, it often tak
the form of disc-shaped patches reser
bling scutula.



FIG. 372.—*Achorion schönleinii*. Colonies 45 days old in maltose agar. (*After Sabouraud in Brumpt.*)

Cultures.—Hanging-drop cultures, as a rule, give very good resul
but ordinary liquid and solid culture-media may be used. The grow



FIG. 373.—*Achorion schönleinii*. Fresh preparation from a 5 days old culture showing the so called "yellow or claviform bodies, *chandler favigues*. (*After Sabouraud in Brumpt.*)

is very irregular: it may, under identical conditions, be slow or ex-
ceedingly rapid. When slow, it commonly gives rise to the develop-

ment of chlamydospores; when very rapid, it is freely ramified, and the mycelium often becomes plastic, giving rise to ameboid forms.

Dysmorphism.—Like most fungi, it is markedly dysmorphic, and this property is so characteristic of the genus that two different growths may be obtained under the same environment. Moreover, the same culture may become so altered in subsequent transplantations that, morphologically, it will be entirely different from the original growth and such variation may become so fixed that a reversion to the original type ceases to occur.

Reproduction.—The dysmorphism of these fungi accounts for the many modes of reproduction that take place; for example: (1) By lateral conidia; (2) by endoconidia; (3) by sprouting; (4) by spindle spores, resembling those seen in *Trichophyton* and *Microsporon*, but not septate and termed by the French "chandeliers faviques" (Fig. 373), from their fancied resemblance to a candlestick; (5) by yellow bodies or "favus claviform bodies," which are 8 to 15μ in diameter, of double contour, and contain a granular protoplasm, and which may properly be regarded as chlamydospores (Fig. 375).

Laboratory Diagnosis.—The laboratory diagnosis is made either by direct examination of the suspected material, as outlined for *Trichophyton*, or by means of artificial culture, as previously described.

Mechanism of Transmission.—*Achorion* belongs to those fungi that, so far as is known, are obligatory parasites, since their saprophytic life in nature has not been ascertained. The transmission of the parasite is, therefore, from man or animals to man by direct contact or indirectly by means of toilet articles.

Pathogenesis.—These fungi are the cause of a definite affection in man and animals known as *favus*. The affection may attack the hair or the glabrous parts of the body, such as the nails, etc.

1. **Achorion schönleinii** (Lebert, 1845).—This species has all the characteristics of the genus as previously described.

Cultures.—Grown on plain agar, this parasite gives rise to an elevated excrescence, irregular in outline, and with ridges on the surface, somewhat resembling the convolutions of the brain. It varies in color from white to light brown. In some instances the growth is variable, either owing to the dysmorphism of the species or because of the age of the culture.

Laboratory Diagnosis.—This can be made either as the result of direct examination of the material or by making a culture of the fungus on ordinary solid media or on maltose agar, as described previously for the genus.

Examination of the Hair.—Viewed under the low power of the microscope (Fig. 371), the hair appears to be irregular in outline, the surface being covered with small, irregular nodules or plaques. When

previously treated with a 30 to 40 per cent. potassium hydroxid solution, the surface appears covered with numerous air-bubbles, which are said to be characteristic of the species. When seen under the high power of the microscope (Fig. 371), both the mycelium and the spores of the fungus, or only the former, are visible. The mycelial elements are seen to invade the interior of the hair, where they appear as straight filaments running from the surface to the center along the axis of the

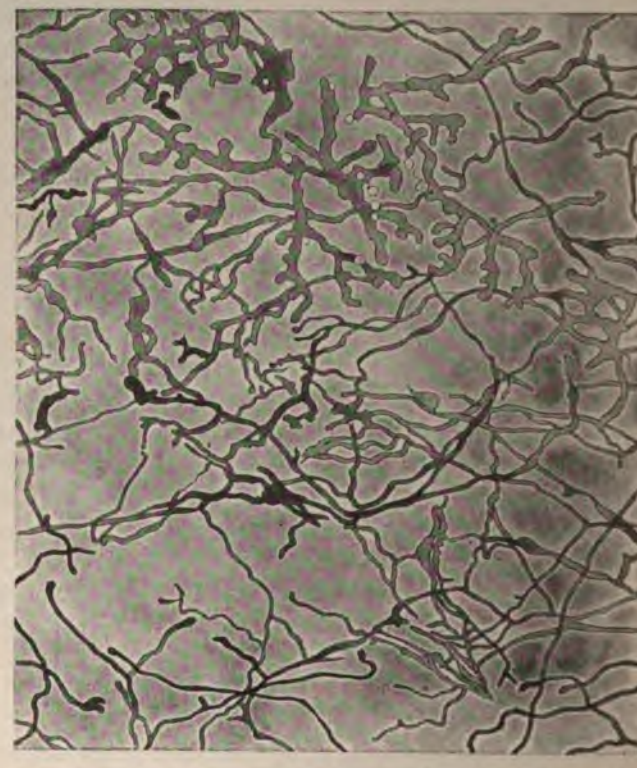


FIG. 374.—*Achorion schönleinii*. Fresh preparation from a 6 days old culture showing amiboid forms. (*After Sabouraud in Brumpt.*)

hair, measuring 2 to 3μ in diameter, and branching dichotomously at points from 12 to 14μ apart.

The mycelial spores are situated in the cortical part of the hair. They are variable in shape and measure from 2 to 5μ. The filament often ends in 3 or 4 short branches, resembling in outline the skeleton of the foot. In stained preparations these filaments are seen to consist in the center of a chromatic substance and an achromatic membrane, which, because of the fact that as it does not take the stain and consequently is not distinctly visible, was formerly believed to be

absent and—hence, as previously stated, the name, *Achorion*, given to the genus.

The Achorion is readily differentiated from *Trichophyton* by simple microscopic examination. The following table shows the characteristic differences between the conditions produced by tbe two fungi:

DIFFERENTIAL CHARACTERISTICS BETWEEN ACHORION SCHÖNLEINII AND TRICHOPHYTON

	Achorion Schoenleinii	Trichophyton
Hair.....	Less brittle and breaks in longer segments, 1 to 2 cm. from orifice of hair-follicle.	Very brittle and breaks in short segments, 3 to 4 mm. from orifice of hair follicle.
Infection.....	Fungus less abundant and does not invade the whole substance of the hair, but leaves non-infected areas.	Fungus very abundant, and invades the whole substance of the hair, which it almost completely replaces.
Mycelium.....	Filaments much longer and less abundant; spores located in cortex of the hair.	Filaments very short and abundant, and spores on the surface of the hair.

Pathogenesis.—It is the cause of a definite affection in man known as *favus*, and is also seen in the lower animals. According to Sabouraud, there is only one species of Achorion, but other authors, such as Neebe, Unna, etc., recognize several varieties. No fewer than nine have been described, of which *A. schönleinii* is the most common cause of favus in man. The lesions appear in the form of peculiar, disc-shaped crusts called *scutula*, which are yellowish in color and give off an offensive odor. The disease is not amenable to treatment and is very contagious.

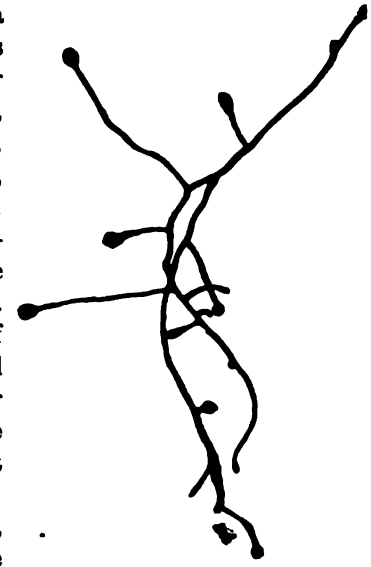


Fig. 375.—*Achorion schönleinii*. Preparation from artificial culture 5 days old showing "favus claviform bodies" (*chandeliers favigues*). (*After Sabouraud in Brumpt.*)

2. **Achorion gypseum** (Bodin, 1907).—This fungus is also the cause of favus in man, and apart from the affection it produces, it is important because of the fact that it manifests transitional characteristics between the genera *Achorion* and *Microsporon*, these characteristics being shown in the cultures. Inoculation of this species into the lower animals produces lesions typical of favus, and resemble those produced by *A. schönleinii*.

FAMILY PERISPORIACEA

The fungi of this family are characterized by the shape of the fruit-body or sporangium, which is usually terminal, and in which the ascogenous hyphæ are, in the early stage, inclosed in a compact envelop, the *perithecium*, made up of interwoven sterile filaments. When mature, the perithecium ruptures and the spores are set free; before disassociation of the spores takes place, however, they may be seen to form chains that are attached radially to the columella (*Aspergillus*), or in brush or pencil-like form (*Penicillium*) at the end of the aërial filament. Reproduction takes place by means of conidia. The family comprises the genera *Penicillium* and *Aspergillus*, which contain species that are parasitic on man.

Habitat.—Of the fungi that are parasitic on man, the *Perisporiacea*, like the *Mucoraceæ*, are found abundantly in nature as saprophytes. They may be said to be merely accidental parasites in man and animals. They are found most frequently on the surface of the body or in the normal body cavities, and only under certain conditions are they seen in the deeper layer of the skin or in the internal organs, such as the lungs.

Culture.—The species of this family are, as a rule, easily grown on ordinary liquid and solid media containing maltose or dextrose, and also on the medium of Roulin. Dysmorphism is less marked in this than in any of the other parasitic fungi.

Pathogenesis.—These fungi are the cause of mycosis of the skin, ears, nose, eyes, lung, etc.

Genus Penicillium (Link, 1809)

Mycelia abundant and septate. Conidiophore hypha with terminal verticillate branches ending in slender, fusiform formations, or *sterigmata*, to which the chains of conidia are attached. The entire spore-bearing hypha with its sterigmata and conidia, resembles a small brush or hair-pencil, from which the genus (*Penicillium*, pencil) derives its name. These fungi are commonly saprophytes, only a few and these unimportant species having been found as occasional parasites on man.

1. **Penicillium crustaceum** (Link, 1763).—This is the fungus commonly found on bread, fruits, and cheese, in the manufacture of which it is often used. It is also known as *P. glaucum*, and is very abundant in nature. The conidia of this species are spheric and about 4μ in diameter. The fungus grows well in ordinary culture-media at a temperature anywhere between 20° amd 35° C. It is very resistant to heat. Like *Bacillus subtilis*, it is a frequent source of contamination in the laboratory. It has been found in man in association with other bacteria in cases of otitis media.

2. **P. minimum** (Siebenmann, 1889), found in a case of otitis media.

3. **P. montoyai** (Castellani, 1907), found in a case of pinta.

4. **P. barbæ** (Castellani, 1907), found in mycosis of the face.

5. **P. bouffardi** (Brumpt, 1906), found in a case of mycetoma, etc.

Genus Aspergillus (Micheli, 1725)

This genus resembles *Penicillium*. The species are differentiated by the structure of the fruit-body. The conidiophore hypha, instead of being branched, terminates in a rounded body covered, while young, by the perithecium; later the perithecium ruptures and the spores



Fig. 376.—*Penicillium crustaceum* (glaucum). Preparation from artificial culture. 1, Bifurcation of sporangiospore; 2, sterigma bearing spores; 3, conidiospores. (× 440 *after Brumpt.*)

are set free. Inclosed in the perithecium are numerous claviform elements (*sterigmata*), attached to the round columella, each giving rise to a chain of round conidia. Like the species of the genus *Penicillium*, those of *Aspergillus* are commonly saprophytic, but under certain conditions they may become parasitic. They usually grow on ordinary media and are dysmorphic; that is, when growing as parasites in animal tissue, their typical morphology is lost and they appear in the form of yeast fungi, oïdia, chlamydospores, or actinomyceticlike organisms. The following are some of the species that have been found to be parasitic on man:

1. **Aspergillus fumigatus** (Fresenius, 1775).—This species is found most frequently as a saprophyte in nature, growing on decayed leaves,

cereals, fruits, in the soil, etc. It is easily cultivated on solid media, where it produces a brown or brownish-green growth. The mycelial filaments are somewhat branched, and hyphæ are septate and from 2 to 3μ in width. The conidiophores are thicker (2 to 5μ), and the sterigmata are about 6μ in length. The spores are round and from 2.5 to 3μ in diameter.

Pathogenesis.—This is the fungus most commonly found in man in cases of aspergillosis of various organs, such as the lungs, ears, nose, eyes, etc., and in wounds. The pathogenic action of the fungus is chiefly mechanical, although, according to Lucet, Ceni, and Besta, it produces a ferment or toxin that has a deleterious action upon the muscular and nervous system of dogs.



FIG. 377.—*Aspergillus fumigatus.* Preparation from artificial culture. × 175. (*After Brumpt.*)

2. **A. niger** (Tisyhan, 1876), found occasionally in mycosis of the lung, ear, etc.

3. **A. barbæ** (Castellani), found in mycosis of the beard.

4. **A. bouffardi** (Brumpt, 1905), found in black mycetoma.

5. **A. pictor** (R. Blanchard), found in pinta, etc.

Remarks on Aspergillosis.—Although the fungi belonging to the genus *Penicillium* are rare in man and animals, those of the genus *Aspergillus* are somewhat common in dogs, birds, and laboratory animals.

In man, aspergillosis of the lung produces pseudo-tuberculosis and pseudomembranous and ulcerative lesions.

ORDER HYPHOMYCETES

Genus Discomyces (Rivolta, 1870)

Mycelia not septate, very fine, resembling bacterial filaments (schizomycetes), without a distinct nucleus. The mycelial filaments terminate in a club-like formation and show a radial arrangement, hence the name, *ray fungi*, applied to certain species. The mycelia give rise to peculiar sporoid granules that are not uncommonly acid fast. These fungi are facultative parasites in man and animals. The first species of the genus, discovered by Bollinger and Harz in a tumor of cattle, was named *Actinomyces bovis;* Blanchard suggested the generic title Discomyces.



Fig. 378.—*Actinomyces of the cornex jaw. (After R. Blanchard in Brumpt.)*

1. **Discomyces bovis** (Harz, 1877).—This is commonly known as the ray fungus, and is the cause of "big head" "lumpy-jaw," or *actinomycosis* in cattle. It may also infect man, in whom it produces similar lesions, and may also give rise to *actinomycotic mycetoma.* The fungus is found as a saprophyte in nature, but may live as a parasite in most tissues and organs, where it gives rise to degeneration and suppuration. The morphology of the fungus varies with its evironment.

Seen as a parasite in the pus discharged from the lesions of actinomycosis, the organism appears in the form of soft yellow granules, the so-called "*sulphur grains,*" consisting of a mass of mycelium. If these grains are pressed between two slides, or examined with the microscope in sections of the lesions (Fig. 379), they are seen to consist of a cortical and medullary zone made of club-shaped hyphæ (10 to 20 by 8 to 10μ), arranged radially. Some authors regard these grains as sterile or degenerated hyphæ, whereas others believe them to be young vegetative forms (Brumpt). The medullary zone consists of a tangle of fine mycelial threads, branched dichotomously, and containing minute mycelial grains or "*sporoids*" that strongly resemble bacteria or micro-

cocci. These minute grains, or "sporoid bodies," may be seen free between the meshes of the mycelium, and not uncommonly show a

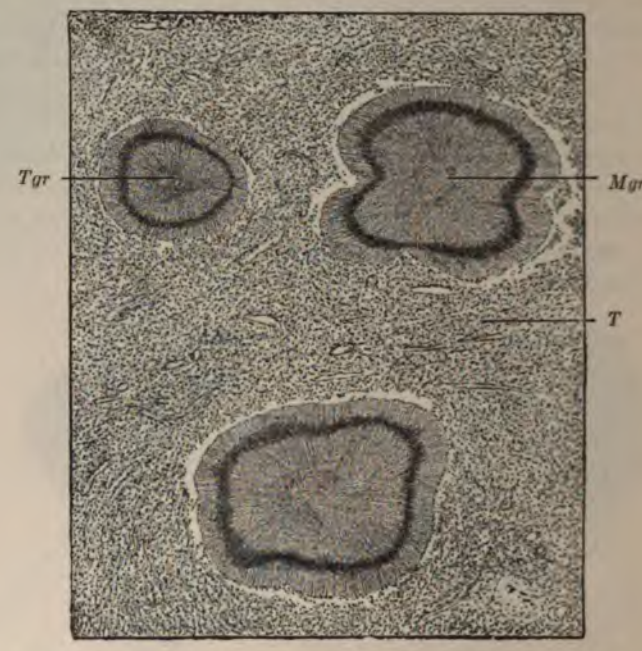


FIG. 379.—*Discomyces somaliensis*. Typical view of a section of a grain of mycetoma. *Tgr*, young grain; *Mgr*, matured grain; *T*, tissue. (*After Brumpt.*)

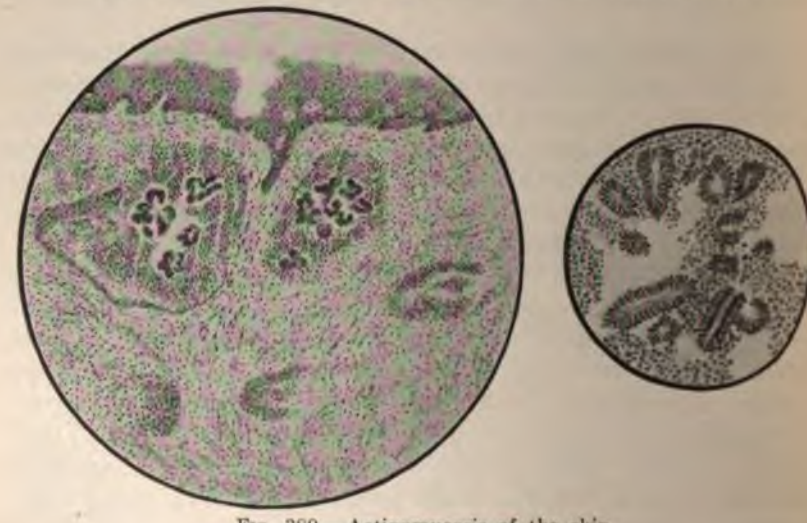


FIG. 380.—Actinomycosis of the skin.

considerable degree of their acid-fast properties. In old grains the center may contain calcareous deposits.

Cultures.—The fungus grows in ordinary solid media at a temperature of from 30° to 38° C. (Fig. 383), and under aërobic conditions it gives rise to delicate filaments, dichotomously branched and non-segmented (Fig. 384). In older cultures these filaments break into short segments containing mycelial grains or spores, resembling bacilli or micrococci. Under anaërobic conditions the growth may assume a bacillary form. In bouillon cultures the fungus gives rise to a floccu-



FIG. 381.—Actinomycosis of the liver.

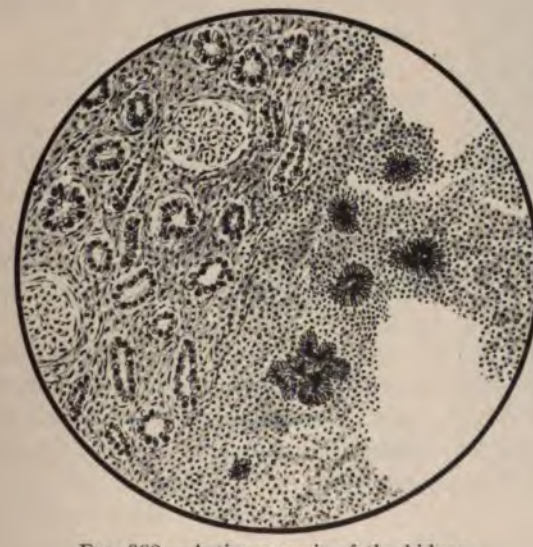


FIG. 382.—Actinomycosis of the kidney.

lent growth that falls to the bottom of the tube, the liquid remaining clear.

Pathogenesis.—The development of the fungus in man gives rise to a tumor-like growth. This condition is known as actinomycosis, and is commonly seen to involve the bones of the face. The parasite may also affect any other part of the body, as well as the internal organs, the lungs, kidney, liver, etc., and the feet and skin (Figs. 379, 380, 381, and 382). The lesions are in the form of tubercules of the granuloma type, containing a necrotic center that commonly undergoes suppuration.



Fig. 383.—Actinomyces bovis, agar culture.

Diagnosis of Actinomycosis.—The discharge from the suspected lesion is carefully examined for minute white or yellowish grains. These are removed, placed on a slide with a little water; another slide is carefully applied to over this, and the grain is crushed gently between the two slides. Under the microscope the characteristic radial growth of the mycelium of the fungus, as previously described, is readily seen. The material can be inoculated into appropriate media for the study of the cultures.

Treatment.—In the early stages potassium iodid internally and local injections of tincture of iodin, in 1 to 2 per cent. solution in glycerin, may give good results. If the lesion is an old one, the growth should be removed.

2. **Discomyces maduræ** (Vincent).—This fungus is the cause of Vincent's pale variety of mycetoma, which is common in Africa and Asia.

3. **Discomyces asteroides** (Eppinger, 1890), found in mycetoma and in abscess of the brain.

4. **Discomyces brasiliensis** (Lindenberg, 1909), found in cases of mycetoma of the leg, etc.

Genus Madurella (Brumpt, 1905)

These fungi are characterized by the formation of an exceedingly fine segmented mycelium, strongly resembling the filamentous growth of bacteria. Reproduction takes place by fragmentation of the mycelium into small segments. The fungi live as saprophytes in

nature, and their growth in man is the cause of mycetoma, with the appearance of black, irregular-shaped grains. The fungi grow readily in ordinary culture-media.

Madurella mycetoma (Laveran, 1902).—This fungus shows all the characteristics of the genus, and, in addition, in an old culture, roundish bodies, 8 to 10μ in diameter, are formed; these are probably chlamydospores.

Pathogenesis.—The growth of this fungus in man is a cause of mycetoma, or Madura-foot. Other parts of the skin beside the feet may also be affected.

Treatment.—Advanced cases require amputation.



Fig. 384.



Fig. 385.

Fig. 384.—Actinomyces bovis. Microscopical appearance of a preparation made from agar culture, stained by Gram.

Fig. 385.—Mycetoma or madura foot. (*After Brumpt.*)

Genus Indiella (Brumpt, 1906)

Hyphæ white, mycelial threads very fine, 1 to 5μ wide, but occasionally thicker (5 to 10μ); they are ramified and septate. Reproduction occurs by the breaking of the filaments into small segments. In old cultures the mycelium forms *sclerotia* containing roundish, chlamydospore-like bodies.

1. **Indiella mansoni** (Brumpt, 1905).—This species has the characteristics of the genus; its growth in man is a cause of pale mycetoma found in India.

2. **I. reynieri** (Brumpt, 1905).—The *sclerotium* is very small (less than 1 mm.), white and coiled. This fungus is a cause of pale mycetoma.

Genus Trichothecium (Link, 1824)

Hyphæ erect, very slender, grouped together, and terminated an oval conidium.

Trichothecium roseum (Persoon, 1801).—This fungus gro as a saprophyte in nature. At first white, it later becomes pink in color. It has been found in cases of otomycosis.

Genus Monilia (Persoon, 1801)

Hyphæ erect, bearing large round conidia at the end.

1. **Monilia montoyai** (Castellani, 1907).—Found in cases pinta. Spores are large and globular (5 to 7μ), and contain a la nucleus.

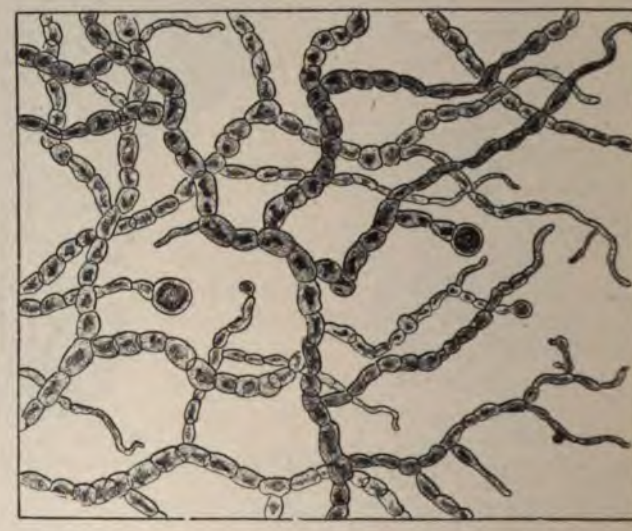


Fig. 386.—*Madurella mycetoma*. Artificial culture. (*After Brumpt.*)

2. **M. candida** (Bonorden), found in white patches of the mouth resembling *thrush*, etc.

3. **M. ashfordi.**—Found in the feces in cases of sprue and regarded as the cause of the disease.

Genus Microsporoïdes (Neveu-Lemaire, 1906)

This genus is important because of its resemblance to the schizomycetes (bacteria). Mycelial threads are extremely delicate (0.6μ), and seldom ramified. They break easily, and the mycelial segments resemble bacilli.

Microsporoides minutissimus (Burehard, 1859).—This fungus has been found in cases of erythrasma. It has not been cultivated.

Genus Sporotrichum (Link, 1809)

Mycelium abundant, septate, and ramified. Conidiospores formed either at the end or at the side of the filament. They are oval or round, and have small sterigmata. Living as parasites, the fungi of this genus may appear in the form of yeast-like cells. The growth of these fungi in man is the cause of a dermatomycosis known as *sporotrichosis*, characterized, as a rule, by the presence of gumma-like lesions.



Fig. 387.—*Sporotrichum beurmanni*. Preparation from artificial culture. 1, Single, lateral conidiospore; 2, terminal conidiospores; 3, collection of lateral conidiospores. × 640. (*After Brumpt.*)

1. **Sporotrichum beurmanni** (Matruchot and Ramond, 1905).—This fungus is easily cultivated in the ordinary culture-media, where it displays the characteristics of the genus. A room temperature is more favorable for the culture of this organism than is the temperature of the incubator.

Pathogenesis.—The growth of this fungus in man is the cause of a mycotic affection known as *sporotrichosis*, a condition that was long confounded with tuberculosis and syphilis.

Diagnosis.—The sporotrichum produces a fungoid affection of the skin and mucous membrane that resembles *syphilitic gumma*, from which it may be differentiated, however, by the fact that although in syphilis the prognosis may be uncertain, in sporotrichosis, with proper

treatment, the patient usually recovers. The Wassermann reaction for syphilis is a valuable point in the differentiation. It should be remembered, however, that there is a possibility of the growth of the fungus occurring on an old syphilitic gumma.

From *tuberculosis* sporotrichosis can easily be differentiated by making a microscopic examination of the material for the presence of tubercle bacilli, or by inoculation of the infecting substance into guinea-pigs. Here again the possibility of the growth of the fungus upon a tuberculous lesion should be borne in mind.

Treatment.—Potassium iodin internally, from 20 to 60 grains daily. The local application of iodized solutions is also to be recommended. Under this treatment the average cases recover in from two to eight weeks.



FIG. 388.—*Trichosporon beigeli*. Chlamydospores forms. *A*, *B*, *C*, chlamydospores as seen in a 6 months-old-culture; *D*, as seen in the lesion, × 150. (*After Vuillemin in Brumpt.*)

2. S. schenki (Hektoen and Perkins, 1900).—This fungus is also a cause of sporotrichosis in man. The organism resembles *S. beurmanni*, from which it can be differentiated only by its action upon sugars and by a few minor morphologic variations in the culture. It ferments the lactose but not the Saccharose. It is believed that this fungus is less pathogenic for mice than is *S. beurmanni*.

GENUS TRICHOSPORON (Behrend, 1890)

These fungi are found as parasites on the surface of the hair, where they reproduce by means of chlamydospore-like bodies, resembling the blastomycetes. They can be cultivated, on artificial media, and in the saprophytic condition (cultures) they form mycelium and either lateral or terminal spores.

Trichosporon giganteum (Behrend, 1890).—This fungus is the cause of *piedra* in Columbia. This disease is a mycotic affection of the hair, characterized by the formation of small, hard nodules, usually light in color, around the hair.

T. beigeli (Rabenhorst, 1867).—This fungus has been found in Europe in nodosities of the hair of the face.

GENUS PITYROSPORUM (Sabouraud, 1895)

Hypha oval or roundish—yeast-like; no mycelium. The genus of this species has not been cultivated.

Pityrosporum ovale (Bizzozero, 1882).—This fungus is probably the cause of pityriasis simplex and pityriasis alba.

Genus Oöspora (Wallroth, 1883)

Hypha septate and very slender forming a mycelium which is more or less compact. Reproduction takes place by means of conidia or chlamydospores. The conidiospore hypha is short and delicate, and ends in a chain of small globular or ovoid conidia. The genus contains a vast number of species, which are but imperfectly differentiated from one another. The best known species is *O. tozenri*.

Oöspora tozenri (Nicholle and Pinoy, 1908).—This fungus has all the characteristics of the genus. It was found in cases of black mycetoma. The parasite can be cultivated in ordinary media, where it reproduces by means of conidia and chlamydospores. When old, the growth assumes a brown or dark color, due to the production of a black pigment by the fungus, which is responsible for the black color of the lesions in man. The parasite is inoculable into pigeons (?).

Genus Oïdium (Link, 1809)

This genus resembles the genus *Oöspora*, and both genera include several species the classification of which is not well determined. The same uncertainty exists regarding other species described under the *Hemispora, Coccidioides*, etc., some of which bear a marked resemblance to the group Ascomycetes, or the genera Endomyces, Saccharomyces, etc., whereas others resemble the Discomyces, etc.

Hemispora stellata (Vuillemin, 1906).—Mycelium abundant; hyppa septate, delicate, hyaline, and unbranched; conidiophore ends in a chain of conidia. In culture the colonies are stellate, irregular in outline, and present a rough surface.

Pathogenesis.—This fungus has been found in man in cases of mycosis resembling sporotrichosis.

Coccidioides immitis (Rixford and Gilchrist, 1899).—In its parasitic existence this fungus resembles yeast-cells. The cells are variable in size, and contain a number of spores in the center. In cultures these spores give rise to mycelial filaments. Reproduction takes place by means of chlamydospores. The fungus is inoculable into lower animals (*Posadas*).

Pathogenesis.—This fungus has been found in mycosis of the skin characterized by the presence of nodular lesions, papules, or pustular eruptions.

Genus Malassezia (H. Baillou, 1889)

Mycelium septate and branched at the end, in T-like fashion. Reproduction occurs by means of conidia, which are sometimes ar-

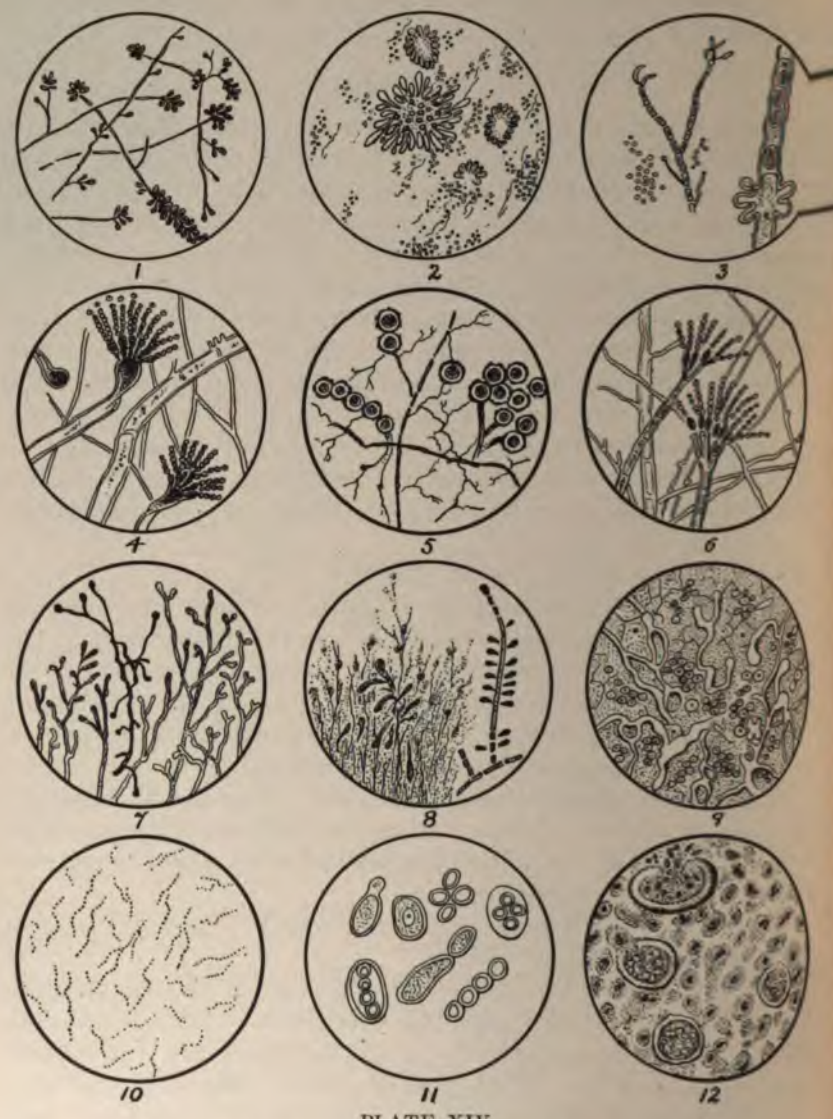


PLATE XIV

The most important pathogenic fungi.

1. Sporotrichum (Gougerot.)
2. Actinomyces.
3. Endomyces (Vuillemin.)
4. Aspergillus.
5. Monilia (Montoya y Florez).
6. Penicillium.
7. Achorion (Sabouraud).
8. Trichophyton (Sabouraud).
9. Malassezia (Fox).
10. Microsporoides (Neveu-Lemaire).
11. Saccharomyces.
12. Coccidioides (Blanchard).

ranged in branches between the mycelial threads. The genus *Foxia* described by Castellani, probably belongs to this genus.

Malassezia furfur (Robini, 1853).—This fungus, also known as *Microsporon furfur*, is the cause of pityriasis versicolor in man. In the lesion it appears in the form of a branched mycelium, or as spheric corpuscular, yeast-like bodies, 3 to 5μ in diameter, and arranged in bunches of from 15 to 30. It is cultivated with difficulty.

Foxia mansoni (Castellani, 1905).—Mycelial filaments not septate, straight, or bent, 2.5 to 3μ in diameter, and unbranched. Reproduction takes place by means of conidia; spores are large (5 to 10μ in diameter), and formed at the end of conidiophores, and not at the side of the filaments; spindle spores are not formed, which serves to differentiate

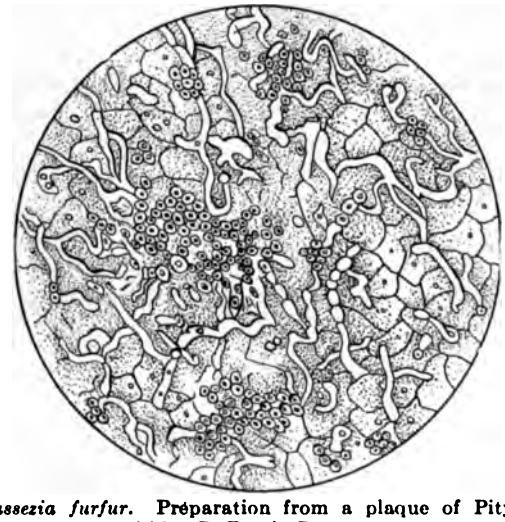


FIG. 389.—*Malassezia furfur.* Préparation from a plaque of Pityriasis versicolor. (*After B. Fox in Brumpt.*)

this species from *Trichophyton* and *Microsporon*. Spores are commonly aggregated in clusters between the mycelial threads. The fungus grows in ordinary solid media, in which it produces black colonies. This parasite is the cause of tinea nigra.

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PART V

APPENDIX

CHAPTER XXVIII

MACROSCOPY AND MICROSCOPY

Dissection.—The Microscope: The Dissecting Microscope; The Camera Lucida; The Projecting Microscope; Measurements; The Ultramicroscope.—Mounting and Preservation of Specimens.—Paraffin and Celloidin Section.—Stains and Reagents.—Staining and Mounting of Specimens.—Microscopic Examination.

Dissection.—In order to make a systematic study of a parasite, as well as to determine the relation that the internal organs bear to one another, and these to the body in general, it is esssential for the student to familiarize himself with the technic of dissection. The instruments and utensils required for this purpose are: (1) A pair of fine-pointed scissors and two pairs of forceps; (2) two dissecting knives, one having a very fine blade and the other being lancet shaped, with two cutting-edges; (3) a pair of dissecting needles; (4) a dissecting tray about 9 by 6 by 1 inch, filled to the depth of half an inch with dark paraffin (a cork board may be used instead of the tray); (5) a dissecting microscope, and (6) a quantity of pins or needles.

In dissecting a worm of fairly large size, such as, for example, *Ascaris*, first determine the ventral surface, which, as a rule, corresponds to the inner coiled portion of the male worm. In the female the median line on the ventral surface is situated between the anus and the vulva, at the junction of the middle and anterior third of the parasite; in the male the median line corresponds to the line between the mouth and the anus and spicules. Second, fix the cephalic end of the worm against the surface of the paraffin in the tray with a pin. Third, fix the caudal end in a similar manner, keeping the ventral side of the worm uppermost. Fourth, cover the parasite with water, and, with the scissors, make a longitudinal incision through the cuticle along the entire length of the worm. Turn the cuticle back and fasten it to the paraffin or cork with pins or needles. Fifth, carefully study the internal organs, which are easily recognized. The same technic is followed for the dissection of other nematodes of average size (Fig. 390).

The dissection of small parasites, such as hook-worm, oxyuris, ticks, fleas, etc., is accomplished with the aid of a dissecting microscope or with the ordinary microscope.

For the study of trematodes in general and the links of cestodes, the object is placed between two slides in a 10 to 40 per cent. solution of sodium or potassium hydroxid. After a few minutes of observation the internal organs are easily distinguished, and appear darker in contrast with the clear appearance of the remainder of the body. If desired, the object may be dehydrated in alcohol, clarified in carbolxylol, and mounted in balsam.

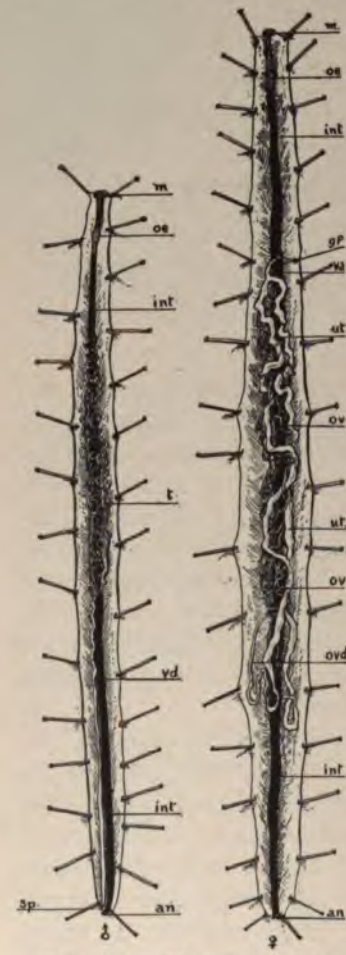


FIG. 390.—Diagram showing the method for dissecting a nematode (*Ascaris megalocephala*) ♂, male; ♀, female. *M*, mouth; *Œ*, œsophagus; *Int*, intestine; *An*, anus; *t*, testes; *Vd*, vas deferens; *Sp*, spicule; *Gp*, genital pore; *Va*, vagina; *Ut*, uterus; *Ov*, ovaries; *Ovd*, oviduct.

For the dissection of a mosquito, the insect should first be killed by tobacco smoke or by the vapor of ether or chloroform passed into a glass jar, test-tube, etc., containing the insect. Second, the wings and legs are trimmed with the scissors or a knife, the insect placed on a microscopic slide and a small quantity of water added. Third, the thorax should be fixed with a dissecting needle, and with another needle the cuticle of the last segment should be broken and then pierced. Both needles should now be gently drawn apart, when the stomach and intestine will appear as a white, tubular structure.

For the dissection of the salivary gland, a section of the head and thorax is first made, as indicated in the accompanying illustration. The remainder of the dissection is carried on under the dissecting microscope (Figs. 391–392).

The Microscope.—The microscope, essentially consists of the following parts: (1) A cylindrical tube, provided at each end with a system of lenses. The one attached to the distal end near the object is called *objective* and the other near the eye, the *ocular*. Commonly there are three objectives, namely, the low, the high and the oil immersion, and correspondingly one or two oculars is all that is required for ordinary purposes. (2) A diaphragm for regulating the amount of light; (3) a *mirror* for the illumination; (4) an Abbe *condenser* between the stage of the micro-

scope and the mirror, which converges the rays of light coming from the mirror toward the object. The focal point of the condenser corresponds to the level of the object when the condensor is screwed all the way up, and for all ordinary purposes it should be kept in this position. The habit of screwing the condenser lower down for darkening the field should be avoided as the diaphragm is intended for such purpose. (4)

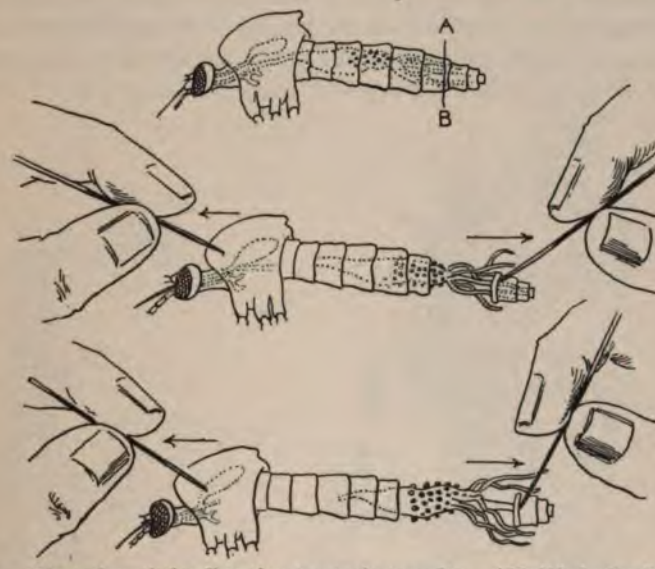


FIG. 391.—Dissection of the digestive tract of mosquito. (*Modified after Blanchard.*)

A gross and fine adjustment for focusing the object. The gross adjustment and the low power should be used first for focusing and selecting the field to be examined, and the fine adjustment and, if required, the high power or the oil immersion, for the study of details, etc.

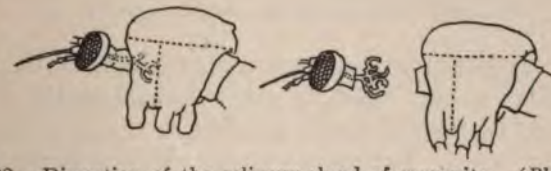


FIG. 392.—Dissection of the salivary gland of mosquito. (*Blanchard.*)

The Dissecting Microscope.—The dissecting microscope consists essentially of the same parts as an ordinary microscope except that it has no condenser, and in addition it is provided with an extra attachment under the ocular for correcting the reversion of the image, so that the observer sees the object as it would be seen directly with the eye (Fig. 393).

The Camera Lucida.—The camera lucida as invented by Wallaston, has undergone various modifications, but essentially it consists of a prism, the section of which is a parallelogram, placed above the ocular in such a manner that the eyes receive the image of the object, this being deflected at the same time at right angles against a mirror which in turn projects it against a sheet of paper placed on the table for the purpose, as shown in Fig. 394. If the tip of the finger or the point of a pencil is now placed on the projected image, this in turn is reflected toward the mirror and to the prism, and then to the eye of the observer, so that both the image of the object under the microscope

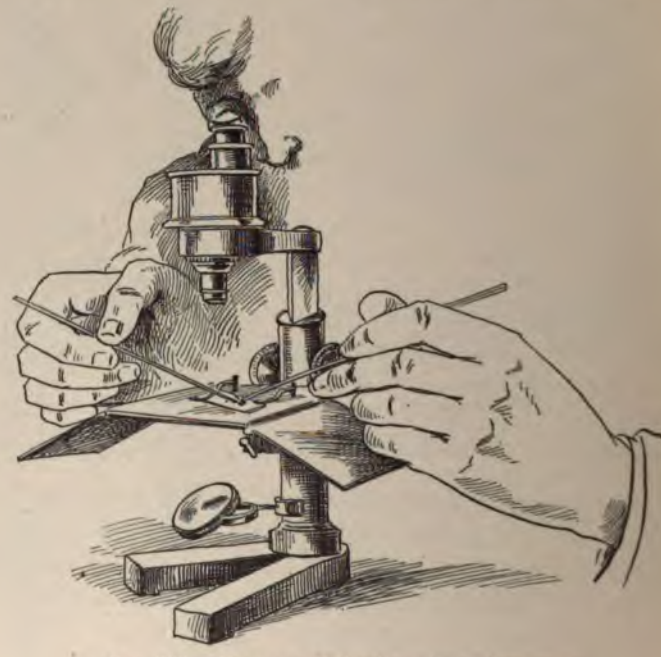


FIG. 393.—Diagram of the dissecting microscope.

and that of the pencil are seen simultaneously upon the paper. In order, therefore, to reproduce an exact drawing of the object under observation, it is necessary merely to follow the outline of the projected object with the pencil. Various cameræ lucidæ are in the market, but the one most commonly used is that of Abbe, which is provided with a series of revolving lenses by means of which the image, as projected upon the paper, may be made more or less distinct, as may be desired. This instrument, however, is far from perfect, and for fine detail is quite unsatisfactory. For securing the general outline of the object and for showing the relation of structures and measurements it is, nevertheless very useful.

The Projecting Microscope.—For all purposes the projecting microscope replaces with advantage the camera lucida, since it can be used for projecting, measuring, and photographing the object. This microscope consists essentially of the same appliances as an ordinary microscope, placed in an inverted position, and as the illumination comes from above instead of from below, the object is projected on a sheet of paper placed below for the purpose, upon which it can be drawn with the greatest accuracy of detail and with a saving of time, or it may be photographed if desired (Fig. 395).



FIG. 394.—Drawing showing the mode of projection by the camera lucida.

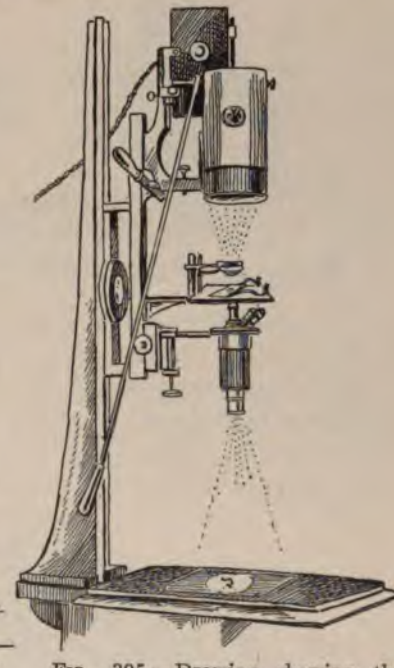


FIG. 395.—Drawing showing the mode of projection by the Edinger apparatus.

A simpler form of this instrument is the projection by a prism, as shown in Fig. 396, in which, by placing the microscope in a horizontal position and applying a mirror to the front of the ocular, the image is thrown on the sheet of paper.

Measurements.—The measurements of objects are taken in the simplest way by using the camera lucida and an objective micrometer. The latter consists of a glass slide containing at the center a millimeter scale divided into 100 equal parts; each division thus corresponds to 0.01 mm., or 10 microns. A micron is, therefore, the one-thousandth part of a millimeter ($\frac{1}{1000}$ mm.) or one-millionth part of a meter ($\frac{1}{1,000,000}$ ml). This micrometer slide is placed under the microscope

and with the aid of a camera lucida the divisions are projected upon a white paper and marked with a pencil. In this way three scales are made: one for the low power, one for the dry high power, and one for the oil immersion. As each of these scales is good only for the combination of ocular and objective with which it was made, it should be so marked to avoid error; the angle of inclination of the mirror (45 degrees)

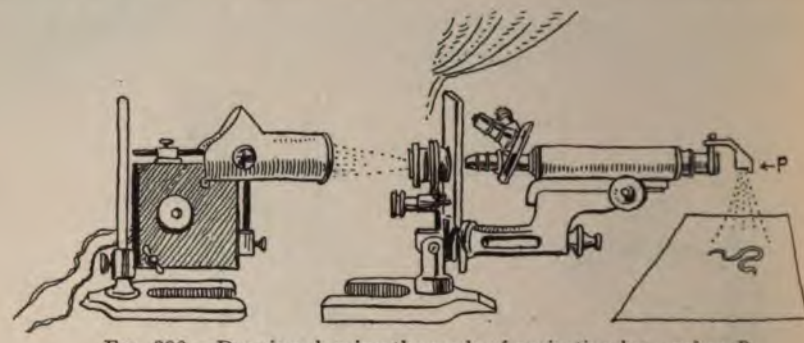


FIG. 396.—Drawing showing the mode of projection by a prism, *P*.

and the distance of the cross-bar should also be marked on the scales, as shown in the accompanying illustration (Fig. 397).

For the measurement of objects such as the eggs of parasites, etc., the image is projected, drawn on the sheet of paper, and measured with the scale. Thus if the distance between the two poles measures seven lines of the scales and the diameter five, since each line is equiva-



FIG. 397.—Illustration showing the method of measuring by scale of an object, such as an egg, projected by the camera lucida.

lent to ten microns, the egg measures 70μ in length by 50μ in width, which is expressed as 70 by 50μ.

The Ultramicroscope.—In the ordinary microscope the objects are seen by transparency or direct illumination, hence they appear as shadows in the field of the microscope. With the ultramicroscope, however, the object is illuminated by oblique or horizontal rays, the result being that they appear as luminous objects on a dark field,

similar to the bright particles seen in a sunbeam in a dark chamber. With this mode of illumination the object appears to be greatly magnified; this is not, however, due to an actual enlargement of the object, for the lenses are the same as those in direct illumination, but to the

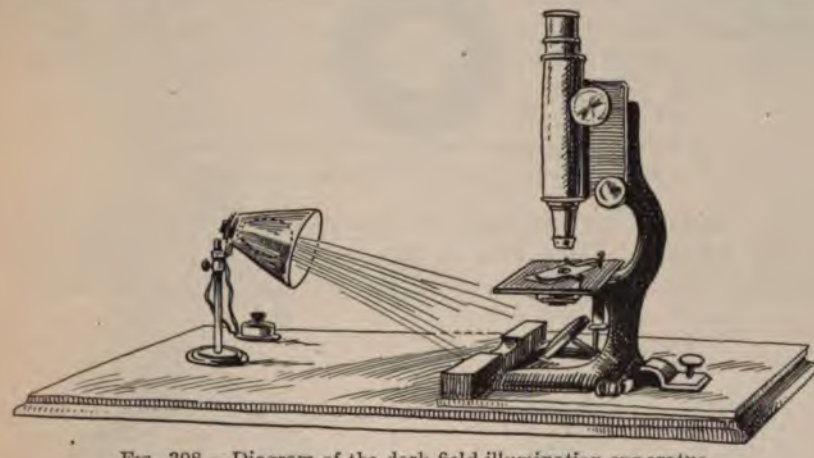


FIG. 398.—Diagram of the dark-field illumination apparatus.

reflection of rays from the object, the result being that particles that are perhaps no larger than a molecule of albumin may be seen as minute luminous bodies, whereas under ordinary conditions objects smaller than 0.2 to 0.5μ are imperceptible under the microscope.



FIG. 399.—Spirochæta recurrentis in the blood of a rat. Dark-field illumination.

Several dark-field illuminating instruments have been recommended, one of which, shown in the accompanying illustration, has the advantage that it can be applied in the place of the condenser, so that

the level of the upper surface of the lens corresponds with the level of the stage of the microscope. A strong illumination, such as the arc-light, should be used (Fig. 398). (1) The field is first properly centered under



FIG. 400.—Cover-glass preparation ringed with asphaltum.

the low power of the microscope by manipulating the screw intended for that purpose. (2) A drop of thin immersion oil is next placed on the top of the lens. (3) The cover-glass preparation to be examined is

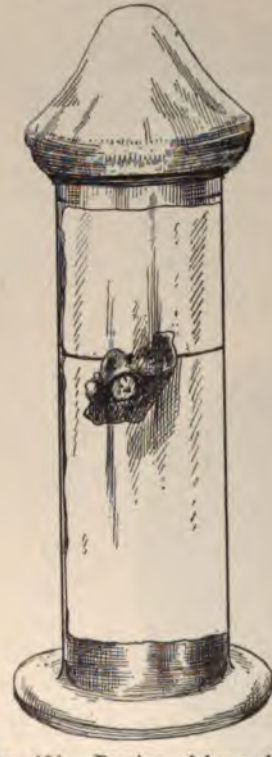


FIG. 401.—Portion of lung showing a nodule containing Paragonimus westermanii, tied to glass plate.



FIG. 402.—Method of mounting a parasite embedded in gelatin on a glass plate.

then placed under the microscope and examined with the oil-immersion objective. (4) Care should be taken to illuminate the field properly so that it is as dark as possible when the floating particles, cells, etc., will appear particularly bright.

In reality the ultramicroscope is of little value for the identification objects smaller than those not seen under the oil-immersion lens of e ordinary microscope by direct illumination, as these minute objects pear merely as bright spots not distinguishable from the inert rticles invariably present in the liquid. For the cytologic study of otozoa, however, and of cells in general, and for the detection of *eponema pallidum* or other allied organisms the ultramicroscope is value (Fig. 399).

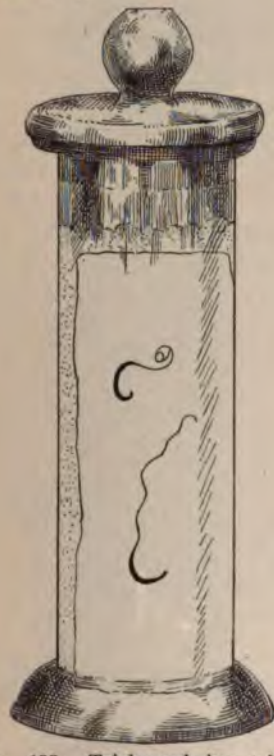


FIG. 403.—Trichocephalus trichuris, unted against plaster of Paris backing.



FIG. 404.—Uncinaria canina in copulation, mounted against plaster of Paris backing.

Mounting and Preservation of Specimens.—For general purposes, parasites and their eggs can be preserved in 2 to 4 per cent. formalin lution, but as this is apt to produce marked hardening of the object, 50 to 80 per cent. alcohol or, better, a 10 per cent. glycerin in 75 per nt. alcohol solution, is to be preferred. A mixture consisting of one rt of acetone and two parts of a 2 per cent. solution of formalin akes an excellent preservative (Smith).

The eggs of parasites may be mounted and preserved in a 2 to 4 r cent. acetic acid solution, in cover-glass preparations, and ringed th asphalt (Fig. 400).

Various methods are recommended for mounting parasites for t museum. If the organism of small size, as, for example, *Paragonim* it may be fixed with a needle, a thread passed through the body, a the specimen fastened to a glass plate. It is then placed in a co tainer, a glass cylinder or jar, which is filled with the preservat solution and sealed with cement. The same method may be emplo for mounting tissues or parasites in general (Fig. 401).

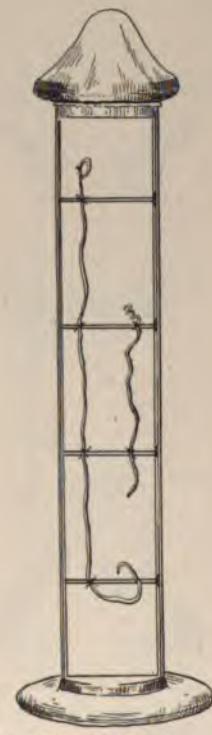


FIG. 405.—Filaria immitis, female to left, male to right. Tied to glass plate.



FIG. 406.—Tænia solium mounted on a glass plate. The head and four terminal segments of the parasite are shown below on the dark ground. ½

Another method consists in first attaching the object to a glass plate with a 30 per cent. solution of gelatin (Fig. 402). The melted gelatin is poured on the dry, clean surface of the glass, and the object is then embedded in the gelatin and placed on the glass plate, where it is allowed to dry for a few minutes, after which it is slowly immersed in a jar containing an acetone-formaldehyd solution, in which the gelatin hardens rapidly and the object becomes attached to the glass.

Numerous bubbles are apt to be given out from the object, and for this reason some time should be permitted to elapse before the jar is sealed.

Weidman has obtained good results by mounting specimens in plaster-of-Paris casts. The method is a simple one, and consists merely in filling, in the horizontal position, about one-third of a cylindric or square jar selected for the purpose. The jar, having previously been stoppered, the plaster is allowed to harden, after which it is separated from the jar, and the parasite is carefully placed between the glass and the plaster. The space between the flat surface of the cast and the wall of the jar is packed with cotton and the container filled with preservative and sealed. The method can be simplified by using only cotton (Figs. 403–404).

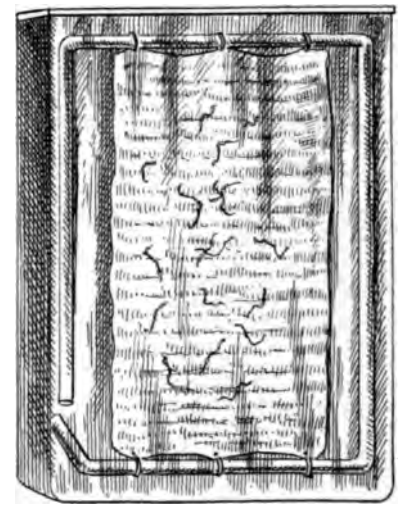


FIG. 407.—Part of duodenum infested with hookworm, showing mounting on glass frame.

Metal or glass frames, beds, or plates can also be used to advantage. On these the parasite, tissue, or organ may be fastened, stretched, looped, or laid (Figs. 405, 406, 407, 408 and 409).

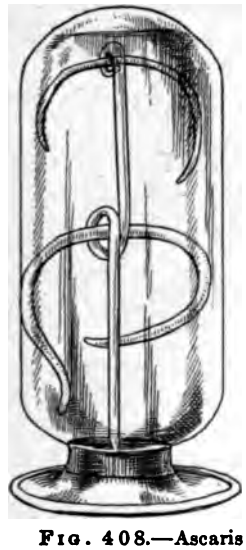


FIG. 408.—Ascaris lumbricoides, the male above, female below, showing mounting on glass rod in inverted jar.

Paraffin and Celloidin Sections.—Briefly stated, the method of procedure for embedding in paraffin is as follows: (1) Place the tissue in 95 per cent. alcohol for six to twenty-four hours; (2) in absolute alcohol for six to twenty-four hours; (3) in chloroform for six to twenty-four hours; (4) in chloroform saturated with paraffin for six to twenty-four hours; (5) in a paraffin bath at 53 to 55° C., two changes, for six to twenty-four hours; (6) embed in paraffin, using nickel or paper boxes, and cool quickly in cold water.

Embedding in celloidin is accomplished as follows: (1) Place the tissue in 95 per cent. alcohol, followed by absolute alcohol and allow it to remain for twenty-four hours; (2) in equal parts of ether and absolute alcohol for twenty-four hours; (3) in thin celloidin for twenty-four hours or longer; (4) mount with thicker celloidin on blocks of vul-

canized fiber or wood; dry for a few minutes in the air; (5) harden celloidin in 80 per cent. alcohol for six hours or longer before cutting. Blocks are preserved in 80 per cent. alcohol. Sections to be embedded should not be over ¼ inch thick.

If the tissue has been fixed in formalin, it should first be softened in running water. Sections are cut with the microtome and should not be more than 6μ and if possible only 2 to 4μ thick.

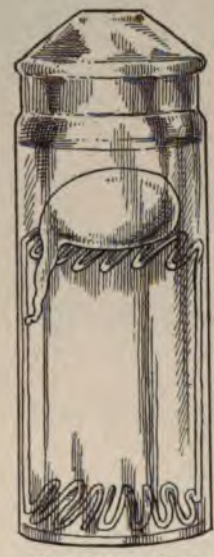


FIG. 409.—*Cysticercus tenuicollis*, the bladder worm of *Tænia marginata* of the dog, showing mounting on glass scaffold.

Stains and Reagents.—Only those stains and reagents most commonly used need be described here.

1. DELAFIELD'S HEMATOXYLIN:

Hematoxylin crystals	4 grams
Alcohol (95 per cent.)	25 c.c.
Saturated aqueous solution of ammonia alum	400 c.c.

Dissolve the hematoxylin in the alcohol and add this to the alum solution. Expose the mixture in an unstoppered bottle to the air and light for three or four days; filter, and add—

Glycerin	100 c.c.
Alcohol (95 per cent.)	100 c.c.

Allow the solution to stand in the light until the color is sufficiently dark. Filter and store in well-stoppered bottles. The stain should be filtered each time before being used. When properly prepared, it should have a purple color and show no precipitate.

2. AQUEOUS SOLUTION OF EOSIN.—There are two varieties of eosin—the one is soluble in alcohol and the other is soluble in water; the latter variety is preferable and is prepared as follows:

Eosin	0.5 gram
Water	100.0 c.c.

This solution is recommended for use after the hematoxylin stain, but as it is apt to deteriorate, it should be made in 25 per cent. alcohol for future use. It is well to filter the solution each time before using it. *When eosin is used before an anilin dye, such as methylene-blue, a 5 per cent. or even a saturated solution should be used.*

3. ALUM OR BORAX CARMIN:

Carmin	3 grams
Alum (or sodium borate)	5 grams
Water	100 c.c.

The solution should be well shaken, allowed to stand over night, and then filtered.

4. BORAX METHYLENE-BLUE:

Methylene-blue	2 grams
Alcohol (95 per cent.)	10 c.c.
Sodium borate (borax)	5 grams
Water	100 c.c.

First dissolve the stain in the alcohol; then add the borax and water and shake well. Let it stand over night and then filter.

Borax methylene-blue is especially useful for staining the *malarial* parasite. It should be diluted in an excess of water, about two to four drops to an ordinary test-tube. Of all the anilin stains, borax methylene-blue is probably the one that gives best results for the staining of nuclear substances and chromatic grains in general.

5. PHENOL CRYSTAL VIOLET:

Crystal violet	1 gram
Alcohol	10 c.c.
Phenol, melted	5 c.c.
Water	100 c.c.

This stain is especially recommended for Gram's method of staining bacteria in spread preparations, tissues, etc. Gram's method is conducted as follows: (1) Make thin spreads of material, dry, and fix in a flame or in absolute alcohol and ether, equal parts, for one or two minutes. (2) Stain with crystal violet for one or two minutes and wash freely in running water. (3) Apply Lugol's solution (Gram) for one or two minutes and wash in running water. (4) Decolorize for a short time with 95 per cent. alcohol. (5) Counterstain with diluted carbolfuchsin for one or two minutes, wash, dry, and mount. The Gram-positive microörganisms (bacteria or fungi), parts of cells (nucleus), etc., appear dark blue, in striking contrast to the Gram-negative objects, which are bright red. For sections proceed as just directed, but permit the stains and Lugol's solution to act for from two to five minutes, and use eosin for counterstaining.

6. CARBOLFUCHSIN:

Fuchsin	2 grams
Alcohol	10 c.c.
Phenol, melted	5 c.c.
Water	100 c.c.

Shake well, and let the mixture stand for a few minutes and then filter, Always filter the solution before using it. The bottle should be kept well corked. This stain is used for staining acid-fast microörganisms. such as tubercle and lepra bacillus. The method or procedure is as follows: (1) Fix preparation in equal parts of alcohol and ether or by rapidly passing it over the flame three or four times. (2) Stain with carbolfuchsin—*cold*—for one to three minutes. (3) Decolorize in

30 per cent. acid alcohol for from fifteen to thirty seconds. (4) in water and counterstain with borax methylene-blue.

7. WRIGHT'S STAIN.—This stain is prepared as follows:

Methylene-blue (Grübler, Höcht, or Koch).....	5 grams
Sodium bicarbonate, 0.5 per cent. solution.....	500 c.c.

Heat the mixture for one hour in the steam sterilizer at 100° C, cool and add—

Yellow eosin, 0.1 per cent. solution.....	2500 c.c.

Collect precipitate on a filter-paper and dry in the incubator. Before using dissolve the precipitate in methyl alcohol in the proportion of 0.1 gram of precipitate to 60 c.c. of methyl alcohol. Keep the bottle containing the alcoholic solution well corked, and replace the alcohol lost by evaporation from time to time as required.

For staining, proceed as follows: (1) Make thin spreads of material, blood, etc., on a slide or cover-glass; dry, and fix in equal parts of alcohol and ether for about two minutes; or, better, the fixing may be made by letting the concentrated alcoholic stain act on the preparation for about two minutes. (2) Without washing the stain add about an equal part of distilled water to the preparation until a metallic film appears on the surface; allow the diluted stains to act for five to ten minutes. (3) Wash in water for about one minute. (4) Dry and mount in balsam or cedar oil, and examine.

The application of diluted borax methylene-blue after the Wright stain will be found to give more striking contrast (Rivas).

8. GIEMSA'S STAIN:

Azur II eosin.....	3.0 grams
Azur II.....	0.8 gram
Glycerin (Merck, chemically pure).....	250.0 c.c.
Methyl alcohol (Kahlbaum I or Merck).....	250.0 c.c.

For use add 10 c.c. of distilled water, 10 drops of stain, and 1 to 2 drops of a 1 per cent. solution of potassium carbonate. The fixed preparation is immersed in this solution for from fifteen minutes to one hour, after which it is washed in water, dried, and mounted.

Both Wright's and Giemsa's stains can be purchased ready prepared on the market. These stains are especially useful for examining blood, blood parasites, and protozoa in general.

9. METALLIC STAINS.—Of the three metallic stains, silver, gold, and osmic acid, only the first need be considered here. Cajal's silver impregnation method, commonly known as Levaditi's method, requires two solutions:

I.	Silver nitrate	2 grams
	Distilled water	100 c.c.
II.	Pyrogallic acid	2–4 grams
	Formaldehyd (strong solution)	5 c.c.
	Distilled water	100 c.c.

This method is especially to be recommended for the staining of *Treponema pallidum* in sections.

(1) Fix the tissue in 95 per cent. alcohol and cut in thin sections, 2 to 3 mm. in thickness. If tissue has previously been fixed in formalin, the section should first be placed in running water for softening, and then in 95 per cent. alcohol for some hours or over night.

(2) Place section in silver solution (I) for three days in the dark at 37° C.

(3) Wash in running water for ten to fifteen minutes and then place section in pyrogallic solution (II) for two days at room temperature.

(4) Dehydrate, embed in paraffin and cut as thin as possible (3 to 6μ).

(5) Fix paraffin section to slide by means of film of albumin on the slide; remove paraffin with xylol, mount in balsam, and examine. The Treponemata appear black and the tissue light yellow or brownish (Plate I).

The following are the reagents and solutions most commonly used:

1. *Physiologic Salt Solution:*

Sodium chlorid (chemically pure)	8.5 grams
Distilled water	1000.0 c.c.

2. *Artificial Gastric Juice:*

Pepsin	0.5 gram
Hydrochloric acid	0.2 c.c.
Water	100.0 c.c.

3. *Lugol's Solution (Gram):*

Iodin	1–2 grams
Potassium iodid	2.0 grams
Water	100.0 c.c.

This solution is stronger than the original employed by Gram. It is used in Gram's method of staining bacteria from cultures or in tissues, as a test for starch, etc.

4. *Acid Alcohol:*

A.	Hydrochloric acid	30 c.c.
	Alcohol (95 per cent.)	70 c.c.

This is used for effecting decoloration in the staining of acid-fast bacteria.

B.	Hydrochloric acid	1 c.c.
	Alcohol (70 per cent.)	100 c.c.

Used for differentiation or distaining of sections.

5. *Carbolxylol:*

Phenol, melted	1 part
Xylol	3 parts

Used for clearing thick sections.

6. *Zenker's Fluid:*

Potassium dichromate	2.5 grams
Corrosive sublimate	5 grams
Water	100 c.c.
Glacial acetic acid	5 c.c.

The potassium dichromate and corrosive sublimate are dissolved in the water by the aid of heat. The acid is added to the stock solution in the proper proportion at the time of using. Tissues fixed in this solution should first be placed in iodin solution (Lugol's) to remove the mercury before dehydration and embedding.

7. *Corrosive Sublimate Alcoholic Solution* (Schaudinn).—Saturated alcoholic solution of corrosive sublimate in absolute alcohol.

Staining and Mounting of Specimens.—For the staining and mounting of protozoa, such as the ameba, fresh material should be selected; that is, material in which the parasites are found to be alive and fairly numerous.

(1) Make thin spreads on a clean slide and fix before it dries in equal parts of absolute alcohol and ether, methyl alcohol, 4 per cent formalin, or saturated solution of mercury bichlorid in absolute alcohol.

(2) Stain with Wright's, Giemsa's, borax methylene-blue, or hematoxylin and eosin.

(3) Wash in water, dry, mount, and examine.

This method is also used for staining trypanosomes, malarial parasites, etc. Giemsa's stain gives the best results. The author has obtained very satisfactory results with Wright's stain, followed by diluted borax methylene-blue. The procedure is very simple, and consists of staining the specimen by Wright's method, as usual, washing in water, differentiating, and staining again with very dilute borax methylene-blue.

For the staining of small metazoa, such as oxyuris, hook-worm, etc., proceed as follows: (1) Fix the parasite in alcohol for twenty-four hours. (2) Wash in water and stain in carmin for from fifteen minutes to one hour. (3) Differentiate in weak acid alcohol for from ten to fifteen minutes. (4) Dehydrate, clear in carbolxylol, and mount in balsam. Links of cestodes can be stained in the same manner.

The staining of paraffin section is accomplished as follows: (1) Fix the section to a clean slide on which a thin film of albumin has been spread, and dry for some hours at 45° to 50° C., or over night in the incubator at 37° C. (2) Remove the paraffin with xylol and immerse

the slide in absolute alcohol for a few minutes, then in 95 per cent. alcohol, and finally in water. (3) Stain in hematoxylin for from five to ten minutes and wash in water. (4) Rapidly decolorize in weak acid alcohol and wash in water. (5) Wash in weak ammonia water for a few seconds and then in water. (6) Stain in water-eosin solution for a few minutes and wash in water. (7) Dehydrate in 50 per cent., 95 per cent., and then in absolute alcohol respectively. (8) Clear in xylol or carbolxylol and mount in balsam.

Microscopic Examination.—In examining any object, such as spreads, sections, etc., under the microscope, it should be made an invariable rule to use the low power of the microscope first for making a general survey of the preparation and for selecting the field, and then examining under the dry high power or under the oil immersion, if desired, for studying the details. If the specimen is a fresh unstained preparation, it will, as a general rule, be found more convenient to close the diaphragm so as to darken the field; in stained preparations, however, the details are brought out more clearly by opening the diaphragm and allowing a sufficient degree of illumination. Of course, no hard and fast rule can be laid down on this point, since it must depend upon the personal experience of the microscopist.

CHAPTER XXIX

BACTERIOLOGY; MYCOLOGY; PROTOZOÖLOGY

Culture-media.—Sterilization.—Isolation of Bacteria.—Identification of the Microörganisms.—Morphologic Classification of Bacteria.—Cultural Characteristics.—Animal Inoculation.—Transplantations and Preservation of Culture.

Only a brief outline of bacteriology will be given here, with special reference to the relation of the subject to parasitology. For a more detailed discussion the reader is referred to the various treatises on the subject.

The knowledge that pathogenic bacteria produce important diseases in man and animals was gained a generation ago, but the fact that parasitic diseases are potent predisposing factors to bacterial infections may be said to be a finding of recent date. A parasitic disease *per se*, when unaccompanied by complications may not be immediately dangerous to the patient, although it may constantly predispose him to a bacterial infection that may eventually end in his death.

Cases of tuberculosis, paragonimiasis, distomiasis, uncinariasis, schistosomiasis, amebiasis, etc., and perhaps even of sleeping sickness, might properly be regarded as mild affections, were it not for the fact that they produce physicochemical changes or ulcerations, etc., in the part affected, or constitutional disturbances in general, as the case may be, thus making the affected part or the entire body a favorable medium for the development of bacteria. This explains the occurrence of cavities or abscesses of the lung in tuberculosis and paragonimiasis; of abscesses of the liver in distomiasis and amebiasis, and of generalized bacterial infection in these and in other affections which, as a rule, is the immediate cause of death.

Bacterial diseases are usually acute and of short duration, ending either in complete recovery of the patient or in death. It may be said that in most cases of primary infection, when uncomplicated, recovery is the rule, but in secondary infection occurring in the course of a parasitic disease, this is usually the exception, owing to the fact that the parasite is a constant predisposing factor to subsequent bacterial reinfections. This would seem to show, therefore, the importance of possessing a fair knowledge of bacteriology in general, and more especially of those pathogenic bacteria that are apt to give rise to complications during the course of a parasitic disease.

It is common knowledge that the air we breathe holds in suspension a great number of bacteria; also that they are present in our daily food and all about us in nature. If one examine a particle of pus, sputum, etc., under the microscope, he may find a variety of these

microörganisms present. Since, as was demonstrated by Pasteur, Koch, etc., these organisms may be isolated and studied by special methods of artificial culture, a knowledge of the nutritive medium and conditions best adapted for their growth is of primary importance.

Culture-media.—From the several culture-media commonly used for the study of bacteria, only a few will be described here as being most suitable for our purpose; these include bouillon, trypsinized bouillon, nitrate bouillon, gelatin, agar, maltose, dextrose, saccharose, lactose bouillon and agar, litmus lactose agar, and litmus milk. These media are prepared as follows:

1. *Bouillon.*—(1) To one pound of veal or horse meat, lean and well chopped, add 1000 c.c. of water and allow it to remain over night in the refrigerator. The meat sugar may be fermented during this time by inoculating the medium with *Bacillus saccharolyticum* (Rivas), but not with *B. coli.* (2) Strain through cheese-cloth and to the meat-juice add 5 grams of sodium chlorid and 10 grams of peptone. (3) Boil for fifteen minutes, neutralize with a 10 per cent. solution of sodium hydroxid, and boil again, using phenolphthalein or litmus-paper as indicator. (4) Replace the water lost by evaporation, filter through a double layer of filter-paper or through absorbent cotton, tube the clear medium, and sterilize by means of the autoclave or by the fractional method.

2. *Trypsinized Bouillon.*—(1) Dissolve 10 grams of peptone in 200 c.c. of hot water; cool to about 45° to 50° C.; add 0.5 gram of trypsin and a pinch of sodium bicarbonate; shake well and incubate in a water-bath at 45° C. for from two to three hours, stirring the mixture every fifteen to thirty minutes. During this incubation the trypsin acts on the peptone, digesting it further, and giving rise to the production of amino-acid or tryptophan. (2) Add water to make 1000 c.c., boil for fifteen minutes to check the action of the trypsin, neutralize and boil again for a few minutes. (3) Filter, tube, and sterilize by means of the autoclave or by the fractional method. For all purposes the trypsinized bouillon is to be preferred to the ordinary bouillon, since it is more nutritious because of the amino-acid it contains; moreover, it is easier to prepare and less expensive.

3. *Nitrate Bouillon.*—To 1000 c.c. of bouillon add 0.2 gram of potassium nitrate; tube and sterilize in the autoclave or in the Arnold sterilizer.

4. *Gelatin.*—(1) To 1000 c.c. of bouillon add 100 grm. of gelatin. (2) Boil for from fifteen to thirty minutes, neutralize, replace the water lost by evaporation, and filter. (3) Tube and sterilize by the fractional method.

5. *Nutrient Agar.*—(1) To 1000 c.c. of bouillon add from 15 to 20 grams of agar cut in small pieces and washed rapidly in running water.

(2) Boil for from thirty minutes to one hour, or, better, melt the a[illegible] in the autoclave at 120 pounds for ten or fifteen minutes. (3) N[illegible] tralize and replace the water lost by evaporation. (4) Filter, tu[illegible] and sterilize in the autoclave or by the fractional method.

6. *Maltose, Dextrose, Saccharose, or Lactose Bouillon.*—To 1000 c.c. of bouillon add 1 gram of maltose, dextrose, saccharose, or lactose respectively. Tube and sterilize by the fractional method.

7. *Litmus Lactose Agar.*—To 1000 c.c. of melted agar add 10 grams of lactose and a few cubic centimeters of litmus tincture until a distinct blue coloration of the medium occurs. Tube and sterilize by the fractional method.

8. *Litmus Milk.*—To 500 c.c. of skimmed fresh milk add litmus tincture until the milk takes on a slight but distinct bluish tint. Tube and sterilize by the fractional method.

9. *Starch Medium.*—To 1000 c.c. of the medium—bouillon or melted agar—add 0.1 to 1 gram of starch, as desired, which has previously been boiled for a few minutes in from 10 to 100 c.c. of water. Mix thoroughly, filter, tube, and sterilize. This medium is exceedingly useful in determining the production, by bacteria and fungi, of diastasic and inverting ferments; this can be determined by applying the iodin reaction to the culture after it has been allowed to grow for some days.

Remarks.—It is essential that all culture-media (bouillon, gelatin, agar, etc.) be clear before tubing. If necessary, the medium can be clarified by adding the whites of two eggs, well beaten in cold water, to one liter of the medium, cooled to 60° C. or lower, then boiled for ten or fifteen minutes and filtered.

It is also most important that *all media be incubated for forty-eight hours at 37° C. after sterilization, in order that any possible contamination may be detected before the medium is used.*

Sterilization.—There are two methods of sterilization, namely: (1) By dry heat and (2) by moist heat.

1. *Dry Heat.*—This consists in sterilization in the oven at a temperature of 150° C. for thirty minutes or at 200° C. for ten or fifteen minutes. A convenient and practical method is to place a small portion of white cotton inside of the oven and another outside, on the top, and compare the two from time to time during sterilization. When the cotton within the oven is slightly browned, sterilization is complete. Dry heat is used for the sterilization of glassware.

2. *Moist Heat.*—This consists in sterilization by steam, either at a temperature of 100° C., by means of the Arnold sterilizer, or at higher temperature, from 110° to 120° C. by means of the autoclave under pressure. Sterilization by the Arnold sterilizer is effected by the fractional method at 100° C. for from fifteen to thirty minutes each day, leaving the medium at room temperature between the intervals.

Sterilization can be accomplished in one day as follows: (1) Prepare the medium as early as possible in the morning and sterilize at 100° C. for fifteen minutes. (2) Incubate at 37° C. for from six to eight hours, during which time the spore germinates. (3) Sterilize again in the Arnold sterilizer at 100° C. for from fifteen to thirty minutes late in the afternoon, and allow the medium to remain in the incubator over night at 37° C., in order to detect any possible contamination. We have found this method, when carefully followed, to be very expedient and satisfactory.

Sterilization by means of the autoclave is effected by heating the medium at 110° to 120° C. for fifteen or twenty minutes. This method has the advantage that sterilization can be completed in a short time; otherwise, for all purposes, in the absence of an autoclave, the Arnold sterilizer will suffice.

Rules for the Sterilization of Culture-media.—Sterilize all media containing sugars, starch, coloring-matter, or gelatin by the fractional method; for all other media use the autoclave, if desired.

Isolation of Bacteria.—If the material to be examined contains many bacteria, it should first be diluted with sterile salt solution or bouillon, and 0.1 to 1 c.c. of the dilution plated on melted agar (either plain agar or litmus lactose agar, or both). The plates should be incubated at 37° C. for from twenty-four to forty-eight hours, after which the isolated colonies should be transplanted in liquid and solid media for identification.

Identification of the Microörganisms.—Identification of the bacteria is made by studying the morphology, cultural characteristics, and virulence of the microörganism.

Morphology.—Although the morphology of bacteria in general is varied, and while even the same species may, under certain conditions, present different forms, three types especially are recognized: Coccus, bacillus, and spirillum. These present some variation in the types according to shape, grouping, etc., as shown in the following table and in Plate XV:

MORPHOLOGIC CLASSIFICATION OF BACTERIA

Spheric (coccus)	Single	Micrococcus.
	Arranged in pairs	Diplococcus.
	Arranged in bunches	Staphylococcus.
	Arranged in chains	Streptococcus.
	Arranged in tetrads	Tetracoccus.
	Arranged in bales	Sarcina.
Rod-shaped (bacillus)	Slightly longer than wide	Bacterium.
	Distinctly longer than wide	Bacillus.
	Arranged in chains	Streptobacillus.
Spiral (spirillum)	Single	Vibrio.
	Arranged in chains	Spirillum.

Cultural Characteristics.—The cultural characteristics of bacteria are generally understood to imply the property these microorganisms possess of effecting changes in the medium in which they grow. This is due to the action of certain substances called ferments or enzymes produced during the metabolic activity of the bacteria. These ferments are of various kinds, such as the *diastases* which change starch into sugar; *inverting* which convert sugar of saccharose into glucose; *sugar splitting*; *proteolytic* which change albumin into peptone, etc. They may produce any of the following changes:

1. *Conversion of the raw organic matter, such as starch, albumin, gelatin, etc., into assimilable or predigested substances, such as saccharose, glucose or peptone respectively.*

2. *The splitting up of organic compounds, such as glucose or proteins, into their elements. Thus* $C_6H_{12}O_6$ *glucose, when acted upon by B. coli, may give rise to* C_2H_5OH *alcohol,* $-CO_2$ *carbon dioxid, or to* $C_2H_4O_2$ *acetic acid or* $C_3H_6O_3$ *lactic acid. Proteid substances, as, for example, peptone, albumin, etc., may be split up into their elements, H, O, N, S, C, etc., and these may combine to form ammonia, sulphurated hydrogen, carbon dioxid, etc., or remain as free H, O, N, etc.*

(3) **Precipitation and coagulation of proteid substances, such as casein in milk, for instance, are produced either by the production of acid in the medium or by the action of a special ferment—rennin.**

(4) **Reduction of nitrate into nitrite, or vice versa: oxidation of nitrites into nitrates.**

(5) Production of pigment or coloring-matter. The chromogenesis of bacteria is best obtained in solid media and in the presence of oxygen.

The table below, in which the morphologic and cultural characteristics of *Bacillus subtilis*, *B. anthracis*, and *B. coli* are given as examples, will be found convenient for use in the identification of bacteria.

TABLE FOR THE STUDY AND

No.	Morphology, Staining, etc.					Cultural						
						Trypsinized Peptone Bouillon. Nitrate Bouillon						
	Shape	Motility	Gram	Acid fast	Spore formation	Clear	Cloudy	Production of Indol	Reduction of Nitrates into Nitrites	Starch Inverted into Glucose	Saccharose Acid production	Saccharose Gas production
1	Bacillus	+	+	0	+	+	0	0	0	0	+?	0
2	Bacillus	0	+	0	+	+	0	0	0	0	+?	0
3	Bacillus	+	0	0	0	0	+	+	+	0	+	+*

Isolation and Identification of Fungi.—For the study of the fungi the method pursued is similar to that outlined for the study of bacteria, except that while a study of the cultural characteristics of bacteria in general is indispensable for their identification, in fungi, on the contrary, the morphology, that is, the character of the mycelium, mode of sporulation, etc., serves as the basis for their identification (Plate XIV). The morphology of the fungi should, however, be studied in artificial cultures, and not as found in the tissues or organs of the body, where, as stated in previous chapters, these plants are apt to show so marked a degree of dysmorphism as to make their identification almost impossible.

As fungi in general are more resistant than bacteria to antiseptics, the material (hair, skin, etc.) may previously be washed in absolute alcohol for a few minutes before it is inoculated in artificial culture-media. By observing this precaution a large number of bacteria that commonly interfere with the growth of the fungi are eliminated. The culture is preferably made in solid media, either plain, maltose, or dextrose agar, and incubated at 30–35° C. or at room temperature with a sufficient supply of oxygen and moisture.

Isolation and Identification of Protozoa.—Three protozoa may be artificially cultivated: namely, ameba, trypanosoma, and treponema.

Cultures of Ameba.—Up to the present time no pathogenic ameba has been cultivated artificially. For the isolation of *Ameba coli* the material (feces containing the parasite), is inoculated into a twenty-four-hour-old agar culture of *Bacillus coli* or *B. typhosus* and incubated at 37° C. The culture is examined daily, and when evidence of growth appears, it is transplanted to fresh media from time to time for some days or weeks.

For the elimination of some of the many bacteria that commonly grow in symbiosis with the amebæ Craig has devised the following method: (1) Transplant the culture on the center of an agar plate

IDENTIFICATION OF BACTERIA

Characteristics							Remarks	Species
lon, etc.		Gelatin	Litmus Milk			Agar		
Dextrose							Pathogenesis Virulence Dysmorphism Agglutination, etc.	
Acid production	Gas production	Peptonized	Acid production	Coagulation	Peptonisation of Casein	Chromogenesis		
+?	0	+	+?	+?	+	0	Not pathogenic	*B. subtilis.*
+?	0	+	+?	+?	+	0	Pathogenic	*B. anthracis.*
+	+	0	+	+	0	0	Not pathogenic (?)	*B. coli.*

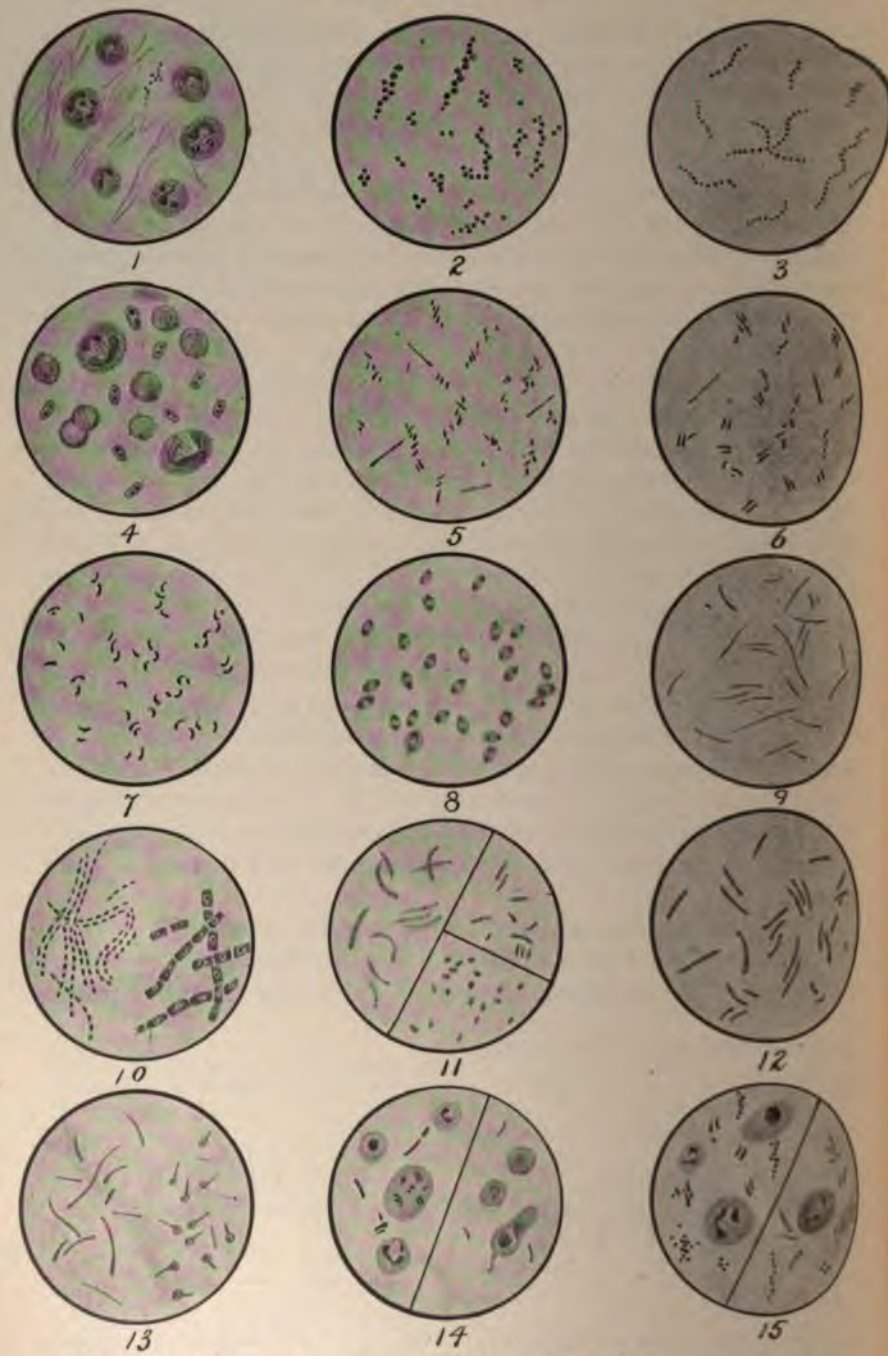


PLATE XV.—The most important pathogenic bacteria. 1, Gonococcus; 2, Staphylococcus; 3, Streptococcus; 4, Pneumococcus; 5, Bacillus coli; 6, Bacillus typhosus; 7, Cholera bacillus; 8, Bacillus pestis; 9; Bacillus pyocyaneus; 10, Bacillus anthracis; 11, Bacillus diphtheriæ; 12, Bacillus mallei; 13, Bacillus tetani; 14, Bacillus lepræ; and 15, Bacillus tuberculosis.

and in concentric rings around the culture inoculate *Bacillus coli* (2) Incubate the plate and examine for several days for the presence of amebæ in the rings. As the amebæ migrate more readily than the bacteria, they may be found in the outer rings, growing symbiotically with pure cultures of *Bacillus coli*. (3) Select the last outer ring in which the ameba is growing and transplant the culture to slant agar.

Cultures of Trypanosoma.—The blood from the heart of a rat parasitized with *Trypanosoma lewisi* is inoculated on slants of blood agar containing a sufficient amount of water of condensation and incubated at 37° C. After a few days evolutional forms of trypanosomes, such as Crithidia and Herpetomonas, may readily be observed in the culture. These cultures may be transplanted to new media, but this cannot be done indefinitely, since the growth gradually dies out (Rivas).

Cultures of Treponema.—Noguchi's method for the cultivation of *Treponema pallidum* is as follows: Place sterile bits of normal rabbit testes or kidneys at the bottom of long sterile agar, bouillon, or ascitic fluid tubes; cover the surface of the tube with about one inch of sterile paraffin, and incubate at 37° C. for at least forty-eight hours to obviate any contamination. (2) Under aseptic precautions inoculate the material (preferably the pulp of a syphilitic liver from a case of congenital syphilis of a child) into the substance of the tissue in the tube by the aid of a pipet, and incubate for several days or weeks. Growth is visible in the second week. (For further details see Chapter VI.)

The Malarial Parasite.—Bass has succeeded in cultivating the malarial parasite in fresh defibrinated blood (see Chapter VII).

Identification of Protozoa.—Protozoa should, as a rule, be identified by their morphology, as shown in fresh cover-glass or stained preparations made from the organs or tissues of the parasitized animal, and not from cultures, as is the case with fungi. The virulence of certain species of trypanosomes, such as *T. brucei*, *T. equiperdum*, *T. gambiense*, upon white rats, and the non-virulence of others, such as *T. lewisi*, make their differentiation easy, whereas the rigid body and the equidistant arrangement of the spirals of *Treponema pallidum* serve to differentiate this organism readily from the Spirocheta, which have a flexible body and an irregular arrangement of the spirals.

In the case of amebæ, it may be said that *the diagnosis should be based on the examination of fresh material* under the dry high power, or preferably under the oil-immersion lens of the microscope. *Fresh cover-glass preparations are, as a rule, to be preferred to the fixed and stained specimens.* Amebæ may appear either in the vegetative or in the encysted form. Pathogenic amebæ, such as *Endameba dysenteriæ*, *E. gingivalis*, etc., *form few pseudopods, usually singly, seldom more than two being produced, and these being of the lobose type;* on the other

hand, saprozoitic amebæ, such as *E. coli*, may form more than two pseudopods and these may not uncommonly be long and slender. This differentiation is still more marked in the free-living amebæ. In addition, *the ectoplasm and the endoplasm are well differentiated in the parasitic amebæ.* During the examination the preparation should be kept at as near body temperature as possible.

As regards the recognition of amebæ in fixed tissue and stained sections: In order to avoid errors, and waste of time, to say nothing of not adding to the prodigious number of pathogenic amebæ that have been found from time to time in the internal organs and that were erroneously regarded as new species, it will be found safer for the beginner to remember that *in fixed tissues amebæ commonly appear to be globular or oval in shape, have regular outlines, and show a foam-like or alveolar protoplasm containing a small and poorly stained nucleus. The mere presence, therefore, under such conditions of pseudopod-like structures should be regarded as suspicious, since in all probability they are either somatic cells, of the embryonic type* (and in a hyperplastic stage) *or in the stage of degeneration, or some foreign substance, such as the spores of fungi, pollen grains, etc., in the stage of germination.* Such artefacts are not uncommonly found in the lungs, mouth, ear, etc., or in abscess cavities communicating with the exterior of the body.

Animal Inoculation.—Bacteria, fungi, and protozoa are divided into two groups, namely: (1) Pathogenic and (2) non-pathogenic. The term pathogenic is generally understood to imply the property which some of these microörganisms possess of producing morbid changes in the living body of higher animals (the host), in which they live and multiply. The terms pathogenic and parasitic are commonly used synonymously, but the former is generally applied to bacteria, whereas the latter is applied to pathogenic fungi, protozoa, and metazoa.

Non-pathogenic microörganisms, as a rule, are those that are incapable of living and multiplying in the living body of man or animals, but thrive on dead organic matter. The term saprophytes is commonly applied to bacteria and fungi, and that of saprozoa to protozoa belonging to this group.

The pathogenic properties of certain bacteria, fungi, and protozoa serve as a most reliable guide for identification, and in some instances they constitute an important point in the differentiation. Thus, while *Bacillus subtilis* and *B. anthracis* are almost identical morphologically and culturally, the former bacillus is non-pathogenic, whereas the latter is the cause of a fatal disease of man and animals. The same is true of *Trypanosoma lewisi, T. brucei, T. equiperdum*, etc., when inoculated into rats.

For determining the pathogenic properties of microörganisms the

culture or material obtained from a parasitized animal is injected subcutaneously, peritoneally, or intravenously into susceptible animals.

Transplantation and Preservation of Cultures.—Cultures of bacteria should be transplanted about every two or three months. Spore-bearing bacteria, of course, need not be transplanted more than once or twice a year, but cultures of streptococcus, pneumococcus, and especially of gonococcus, die rapidly, and to insure their preservation the growth should be transplanted every few days or even daily in special culture-media (blood-serum, blood-agar, etc.). Fungi in general are more resistant, and need not be transplanted oftener than every three or six months unless the medium shows evidence of dryness. This also applies to spore-bearing bacteria. Cultures of fungi and bacteria are best preserved in tubes sealed with a cotton plug saturated in equal parts of sterile paraffin and vaselin.

Protozoa do not keep well in artificial cultures, with the exception of *Treponema pallidum*, which should be transplanted every one or two months. Cultures of *Ameba coli* should be transplanted once or twice every month. As a rule, most cultures of bacteria and fungi keep well at room temperature.

CHAPTER XXX

HEMATOLOGY AND SEROLOGY

Composition of the Blood.—The Blood Cells.—Hemoglobin.—Color Index.—Blood Preparations.—Blood Counting.—Differential Counting.—Interpretation of Results.—Sero-agglutinins.—Seroprecipitins.—Wassermann Reaction.—Bacteria in the Blood.—Bacteremia.—Primary, Metastatic, and Secondary Bacterial Infection.—Blood Culturing.—Protozoan Parasites.—Metazoan Parasites.—The Cerebrospinal Fluid.—The Technic of Lumbar Puncture.—Cerebrospinal Fluid for the Wassermann Reaction.—Noguchi's Butyric Acid Test.—The Cerebrospinal Fluid in Sleeping Sickness.

The blood, to which Claude Bernard gave the name of the internal medium of the organism, constitutes one of the most important fluids of the body. It is concerned not merely with oxidation, with the distribution of nutritive substances, with the neutralization and elimination of poisons, and with several other important physiologic functions, but also represents a most potent factor in the defense of the organism against infection; it is also concerned with the destruction of pathogenic bacteria and other parasites during the course of disease.

It has been shown, in recent years, that the diagnosis of a larger number of diseases (anemias, bacterial infections, protozoan and metazoan diseases, etc.) can be made with certainty as the result of an examination of the blood, and it is probable that, with an improved technic, the laboratory diagnosis of many other morbid conditions of the body will be rendered possible. It is, therefore, indispensable for the laboratory worker to possess a thorough knowledge of hematology and for physicians in general to be familiar with the means of interpreting the results. Furthermore, it should be emphasized, in this connection, that, while examination of the blood is of so great assistance in diagnosis it possesses the additional advantage of simplicity, since in most instances all that is required is merely a drop of blood, which can easily be procured.

Though some diagnostic methods have but a theoretic interest, others have been demonstrated to be most useful and reliable guides to the diagnosis of disease.

Composition of the Blood.—The blood is made up of a fluid portion, the *blood plasma,* and a semisolid or plastic organized portion, the *blood-cells,* both being present in about equal proportions by volume.

Apart from its inorganic constituents the blood plasma is especially rich in proteins. Under normal conditions it is clear and light amber in color; shortly after meals, however, it is slightly cloudy. Blood

Serum is obtained by allowing the blood to coagulate and then collecting the liquid with a pipet.

The Blood-cells.—There are three varieties of blood-cells: (1) Erythrocytes; (2) leukocytes; and (3) blood plaques.

The Erythrocytes.—Under normal conditions the erythrocytes occur in the proportion of 4,000,000 to 6,000,000 per cubic millimeter of blood. In man these cells are non-nucleated, and measure 6 to 8μ in diameter.

The *Leukocytes.*—Under normal conditions the leukocytes number from 5000 to 10,000 per cubic millimeter; that is, they are in the proportion of about 1 to 2 to 1000 erythrocytes. There are two varieties of white blood-cells: (1) *Mononuclear leukocytes* or lymphocytes, and (2) *polynuclear leukocytes.*

The mononuclear cells are of two kinds: *Large lymphocytes,* which are recognized by the fact that they have a relatively large protoplasm and a pale stained nuclei, and are in the proportion of 3 to 10 per cent.

The *small lymphocytes* are distinguished by a scanty protoplasm and a deeply stained nucleus. They are larger than the erythrocytes, and are found in the proportion of 15 to 25 per cent. in relation to the other leukocytes.

The *polynuclear leukocytes,* or *polylobes,* are intermediate in size between the small and large leukocytes, and are characterized by the presence of an irregularly divided polylobed nucleus and a protoplasm containing small neutrophilic granules. These cells are present in the proportion of 65 to 75 per cent.

There are two other kinds of polynuclear cells: (1) *Eosinophiles,* containing eosinophile grains which contain eosinophile grains in the protoplasm, and (2) *basophiles* or *mastzellen,* containing basic granules. The former are present in the proportion of 0.1 to 3 per cent., and the latter in about 0.1 to 1 per cent.

Still another variety, the *transitional leukocytes,* are recognized. These are characterized by the presence of an irregular nucleus. These cells may properly be regarded either as large lymphocytes or as polynuclear leukocytes, according to the appearance of the nuclei and the size and character of the cytoplasm (Plate XVI).

The Hemoglobin.—The hemoglobin, which gives the color to the blood, is contained in the erythrocytes. The most satisfactory instrument for determining the percentage of hemoglobin is the Miescher modification of the von Fleischl hemoglobinometer; the Gower and the Sahli modification of the Gower hemoglobinometer are also satisfactory instruments; the simple colored discs and filter paper method of Tallqvist may answer the purpose, although this method is not so accurate. For man the normal percentage of hemoglobin is 100 to 110 per cent.; for women it is 80 to 100 per cent., and for children it is 70 to 80 per

cent., which corresponds proportionally to about 5,000,000 to 6,000,000 erythrocytes and 7500 leukocytes for the man; 4,000,000 to 5,000,000 erythrocytes and 7500 leukocytes for women, and 4,000,000 to 4,500,000 erythrocytes and 9000 leukocytes for children per c.mm.

Color Index.—By the term color index is understood the relation that exists between the number of erythrocytes per c.mm. of blood and the percentage of hemoglobin, 5,000,000 erythrocytes being regarded as equivalent to 100 per cent. hemoglobin. To ascertain the percentage (factor) of red cells multiply the first two figures by two; and to obtain the color index divide the percentage of hemoglobin by the percentage of erythrocytes present. In normal blood containing 5,000,000 erythrocytes and 100 per cent. of hemoglobin, the color index is 1.0 that is:

$$\text{Hb } 100 \div \text{blood-cells per cent.} : 50 \times 2 \text{ or } \frac{100}{100} = 1.0.$$

The same is true in abnormal conditions when the hemoglobin and the erythrocytes are both equally diminished, as in anemia following hemorrhage. Thus, if the percentage of hemoglobin is 50 and the erythrocytes number 2,500,000, the color index is:

$$\text{Hb } 50 \div 25 \times 2 \text{ or } \frac{50}{50} = 1.0.$$

In chlorosis the hemoglobin is greatly diminished, whereas the erythrocytes are only slightly decreased in number. In this condition the color index is less than 1.0. Thus, if the hemoglobin averages 60 per cent. and the erythrocytes number 4,000,000, the color index is $60 \div 80 = 0.75$. In pernicious anemia, in which the erythrocytes are greatly diminished, whereas the hemoglobin is proportionally only moderately decreased, the color index is greater than 1.0. Thus, if there is 60 per cent. of hemoglobin and the erythrocytes number 2,000,000, the color index is $60 \div 40 = 1.5$.

It will be seen, therefore, that in the anemias there are three types of color index: (1) The normal type, 1.0, in which both the erythrocytes and the hemoglobin are proportionally decreased, as in the anemia following hemorrhage; (2) the chlorotic type, in which the index is below 1.0; and the (3) pernicious type, in which the index is above 1.0.

Blood Preparations.—There are two methods of making blood preparations—by means of the fresh blood cover-glass and by making spreads of dried and stained blood. The fresh blood preparations are convenient for examining for the presence of large blood parasites, such as the microfilariæ and trypanosomes, but for the detection of the malarial parasites the author has found the dry stained spreads more satisfactory.

The fresh blood cover-glass preparations are made by placing a all drop of the blood upon a microscopic slide and gently applying over-glass to the top of it. The success of the procedure is depend- t largely upon the amount of blood used for making the preparation. properly prepared specimen, as stated by Manson, should show three nes: (1) An empty center, (2) surrounding the center a scattered ne, in which the erythrocytes are found fairly well distributed and

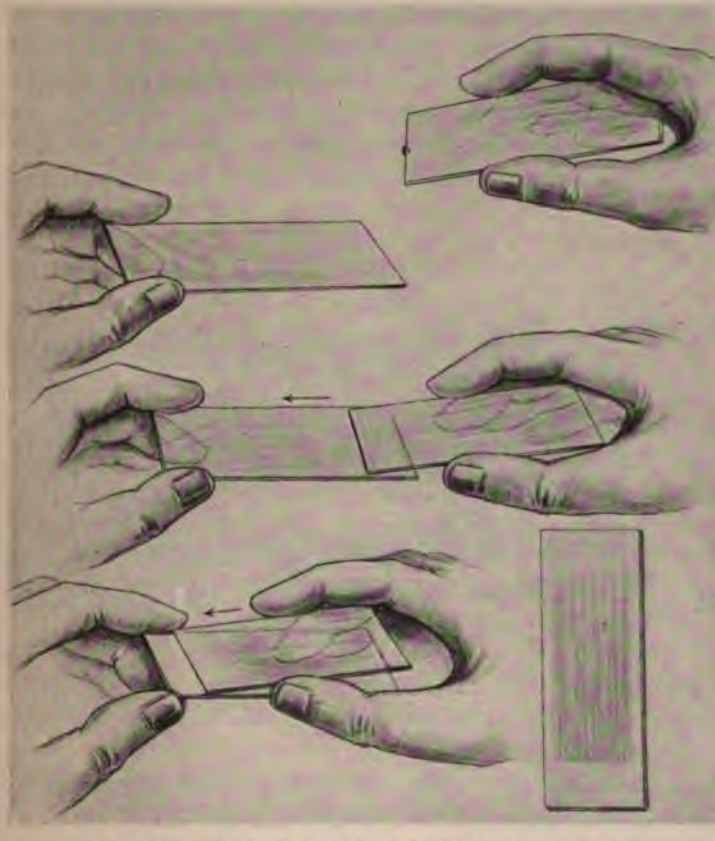


FIG. 410.—Method of making a blood film preparation.

ar to but not touching one another. It is in this zone that the search r malarial parasites and trypanosoms should be made. (3) A icker peripheral zone, in which the cells are found more or less ouped together. It is in this zone that microfilariæ, when present the blood, are more apt to be found.

The dried blood spreads are made either by placing a small drop blood between two cover-glasses and then drawing them apart, by spreading a small drop of blood on a slide with the edge of a

cover-glass or slide held flat against the surface of the slide, and drawing the upper slide either toward or away from the drop of blood, in the manner shown in the accompanying illustration. The latter method gives the best results (Fig. 410).

The slides and cover-glasses should be absolutely clean. The finger from which the blood is to be taken should first be bathed with alcohol. A wise precaution is to dry the preparation as soon as possible by passing it rapidly over the flame.

For staining, diluted borax methylene-blue, Giemsa's, or Wright's stains may be used. For examining for blood parasites, especially for the malarial organism, dilute borax methylene-blue will be found more expedient and satisfactory (Plates I and VI). The preparation is fixed in methyl alcohol or in equal parts of alcohol and ether for one

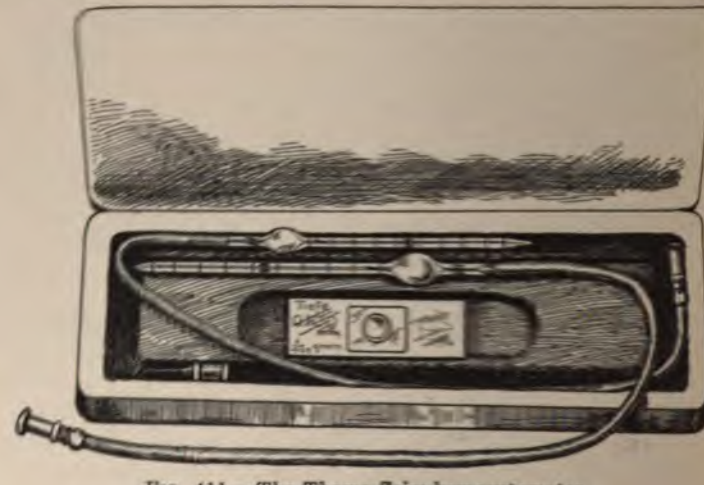


FIG. 411.—The Thoma-Zeiss hemocytometer.

or two minutes and the dilute methylene-blue solution applied for one or two minutes.

Blood Counting.—For counting the cells of the blood the Thoma-Zeiss hemocytometer is generally employed. This instrument consists of a glass slide on which the blood-cells are counted, and two graduated pipets for collecting and diluting the blood; the one is graduated to 101, and is used for counting the erythrocytes, and the other is graduated to 11, and is used for counting the leukocytes. The pipet marked 101 may be used for both countings, if desired, by using for the dilution an isotonic liquid stain, such as Toisson's solution, in which the leukocytes take on a purple stain.

Each pipet consists of a capillary tube, which extends into an ovoid chamber above, and a short piece of rubber tubing with a bone mouthpiece attached to it. The capillary tube is graduated into 0.5 and 1.0

divisions for measuring the desired amount of blood to be taken, and the chamber contains a glass pearl that assists in mixing the blood and the diluting fluid (Fig. 411).

The counting slide has a square glass plate cemented to its surface, and a circular opening in the center nearly filled by a glass disc, 0.1 mm. thinner than the glass plate, so that when the cover-glass is applied, the space between the under surface of the cover-glass and the surface of the disc is 0.1 mm.

The center of the disc is marked off into a square millimeter, divided on the surface by a series of horizontal and vertical lines, twenty in number, on each side, which divide the disc into 400 small squares. Each small square is, therefore, equal to one four-hundredth of a square millimeter. Additional lines divide this surface into quadrants, each quadrant containing sixteen of the small squares inside of the double lines.

The diluting fluids used are: for the erythrocytes, isotonic salt solution and for the leukocytes, 2 per cent. acetic acid solution.

Counting the Erythrocytes.—The tip of the little finger of the left hand, previously washed with alcohol and dried, is pricked with the point of a sterile needle (preferably one that is flattened and sharpened at both edges), and by gentle pressure a fairly large sized drop of blood is gently forced through the opening. Either one-half of the pipet, *i.e.*, up to the mark 0.5, or the entire tube, up to 1.0, is filled with the blood. The tip of the pipet is quickly wiped off with filter-paper, the salt solution aspirated up to the 101 mark, and the mixture shaken for half a minute. Blow out and aspirate the suspension in the depression of a hanging-drop slide, in a watch-crystal, or on the surface of a plain slide, and with the pipet carefully deposit a small drop on the center of the disc of the counting slide. Gently slide on the cover-glass especially made for the purpose, and apply pressure to its side but never to the center, until the "Newton color zones" appear. A properly made preparation should show no dust-particles or air-bubbles; the central disc should be completely covered with the liquid, and the Newton rings should be distinctly visible. Allow the erythrocytes to settle for one or two minutes before beginning the counting.

The method of determining the number of erythrocytes in 1 c.mm. of blood is a matter of personal preference. As a rule, the high power of the microscope is used, and the number of erythrocytes in from 20 to 100 small squares is counted. This number, multiplied by the dilution and by 4000, and divided by the number of squares counted, will give the number of erythrocytes in 1 c.mm. of blood.

$$\frac{\text{Number of erythrocytes} \times \text{dilution} \times 4000}{\text{Number of squares counted}} = \text{Number of erythrocytes in 1 c.mm.}$$

Thus, if 1200 corpuscles were counted in 100 squares, and the dilution is 100, the number of erythrocytes will be

$$\frac{1200 \times 100 \times 4000}{100} = 4{,}800{,}000 \text{ in 1 c.mm.}$$

The author uses a 1:200 dilution by filling the pipet up to the 0.5 mark, makes the counting under the low power of the microscope, and determines the number of erythrocytes counted in 20 or 40 squares by counting the cells found between one or two of two vertical lines, as shown in the accompanying illustration; the number of erythrocytes is multiplied by 40,000 or 20,000, as the case may be, according to the

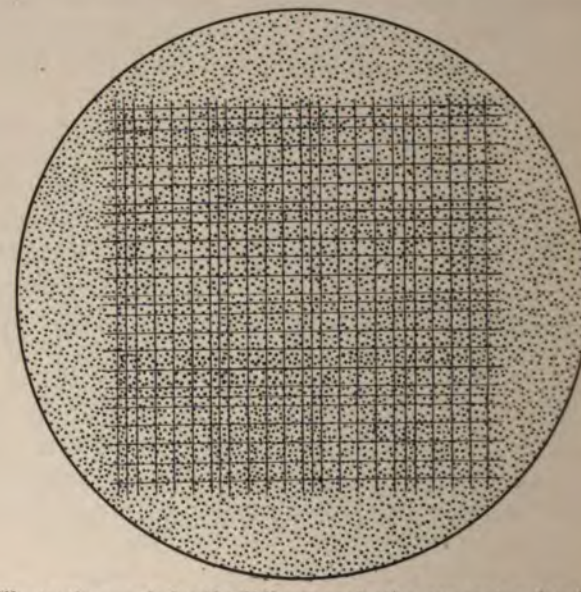


FIG. 412.—Illustration made by the Edinger projection apparatus showing the method of counting the erythrocytes as seen under the low power of the microscope.

dilution and number or square counted and this gives the number of cells in a cubic millimeter of blood.

Thus, if the number of corpuscles in the twenty squares is 130, and the dilution is 1 :200, the number of erythrocytes will be

$$130 \times 40{,}000 = 5{,}200{,}000 \text{ in 1 c.mm.}$$

To avoid counting any of the corpuscles twice, count the cells touching the upper and left side of the square or line, but not those touching the lower and right side.

Counting the Leukocytes.—This procedure is the same as for the erythrocytes, except that the pipet graduated 11 and dilution 1:10 (or 1:20) is used with a 2 per cent. acetic acid solution. Here again,

as in the erythrocytes, for ordinary purposes we use 1:20 dilution, and the number of leukocytes are counted, under the low power of the microscope (Fig. 413), in the entire 400 small squares (that is, in the whole square millimeter), as shown in the accompanying illustration, and the number multiplied by 200 gives the number of leukocytes per cubic millimeter.

Thus, if the number of leukocytes in the entire large square is 30, 30 × 200 = 6000, which represents the number of leukocytes in 1 c.mm.

Differential Counting.—Differential counting of the blood-cells applies chiefly to the leukocytes, and consists in the determination of the percentage in which the different varieties of these cells are found

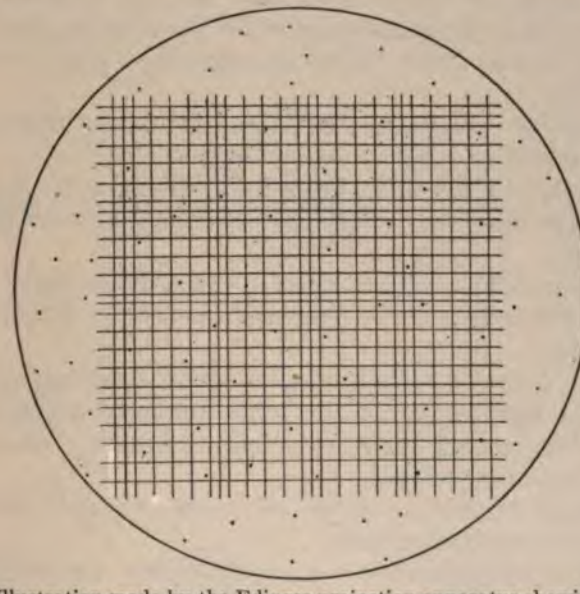


FIG. 413.—Illustration made by the Edinger projection apparatus showing the method of counting the leukocytes as seen under the low power of the microscope.

in the total count made of from 200 to 600 leukocytes. There is no standard of classification of the leukocytes, but for practical purposes those found in normal blood may be said to be of the four varieties previously described, namely: Polynuclear; mononuclear or lymphocytes, both large and small; eosinophiles; and basophiles. These are found usually in the following proportions: Polynuclear, 71 per cent.; small lymphocytes, 20 per cent.; large lymphocytes, 6 per cent.; eosinophiles, 2.9 per cent., and basophiles, 0.1 per cent.

Abnormal Leukocytes.—Besides an abnormal excess in the percentage of any of the leukocytes, the *myelocytes* are not seen normally in the blood. They are large mononuclear leukocytes, containing a

granular protoplasm consisting of neutrophilic, eosinophilic, or basophilic grains, and are known as *neutrophilic*, *eosinophilic*, or *basophilic myelocytes* respectively (Plate XVI).

Abnormal Erythrocytes.—These may be non-nucleated or nucleated. Of the non-nucleated variety, three forms may occur: (1) *Macrocytes* and (2) *microcytes*, the former being larger and the latter smaller than the average normal erythrocyte (6 to 8μ). (3) *Poikilocytes*, which are irregular or ameboid in shape.

Of the nucleated form three varieties may also occur, namely, (1) *macroblasts*, (2) *microblasts*, and (3) *normoblasts*, the names likewise having reference to their size as compared with that of a normal erythrocyte (Plate XVI).

Interpretation of Results.—No fixed rule can be given as to the results obtained in the examination of the blood except when these are sufficiently typical. The following suggestions may, however, be found helpful:

1. *Pernicious Anemia.*—Color index above 1.0; presence of nucleated erythrocytes, macrocytes, and poikilocytes.

2. *Chlorosis.*—Color index below 1.0. Erythrocytes exhibit little change except that they show pale staining. Few nucleated cells may be found.

3. *Anemia Following Hemorrhage.*—Color index about 1.0. Nucleated erythrocytes may be present. Leukocytes possibly slightly above 10,000.

4. *Acute Lymphatic Leukemia.*—Marked lymphocytosis, 50,000 to 500,000 or more per c.mm., the large lymphocytes predominating; a more or less marked degree of pernicious anemia; few myelocytes are not uncommonly present.

5. *Chronic Leukemia.*—Same as acute leukemia except that small lymphocytes predominate.

6. *Myelogenous Leukemia.*—A more or less marked degree of pernicious anemia and leukemia, with the myelocytes predominating.

Sero-agglutinins.—By the term agglutinin is understood the presence, in the blood-serum, of a substance, an antibody, or amboceptor, that has the property of causing bacteria, erythrocytes, and some protozoa, suspended in a fluid, to cohere and to form clumps. These agglutinins may show a specific tendency, as when they agglutinate only one form of cell or microörganism, or a non-specific, as when they agglutinate more than one variety. For example, normal blood-serum may, under certain dilutions, agglutinate almost any form of bacteria.

A striking example of a specific agglutinin is furnished by the serum of typhoid patients, which agglutinates only the *typhoid bacillus*, and although it also agglutinates *Bacillus paratyphosus*, it does so only in a much lower dilution.

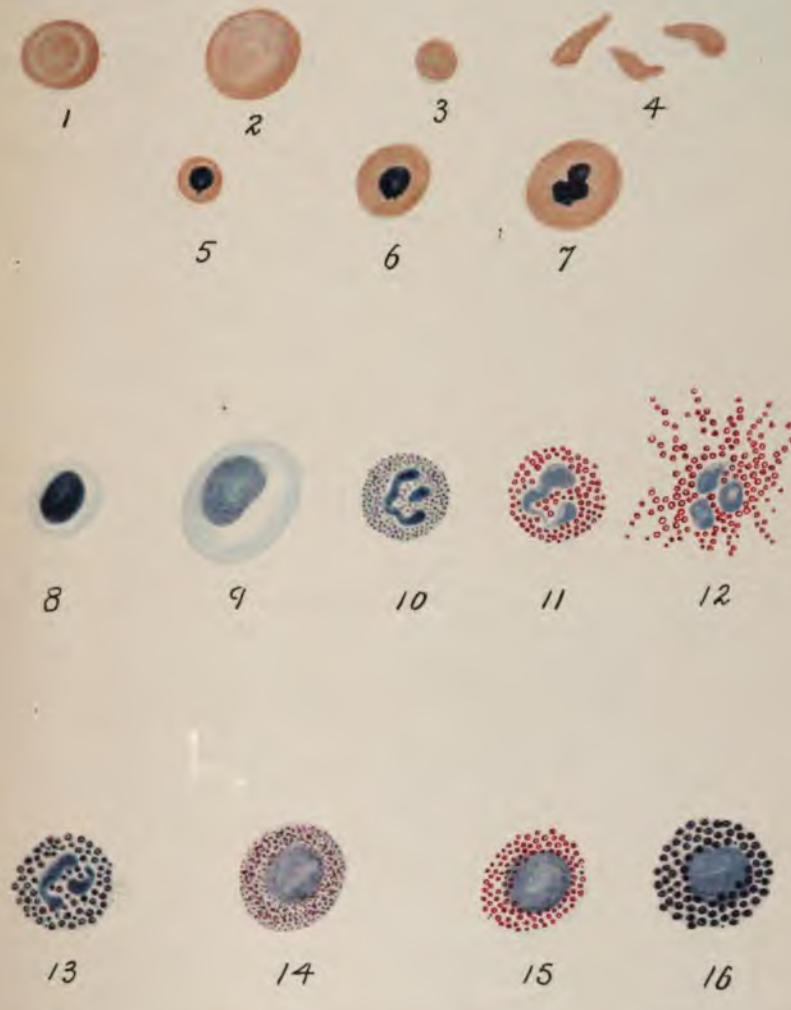


PLATE XVI.—Normal and abnormal blood cells of man. 1, Normal erythrocytes; 2, macrocyte; 3, microcyte; 4, poikilocyte; 5, microblast; 6, normoblast; 7, macroblast; 8, small lymphocyte; 9, large lymphocyte; 10, polynuclear leukocyte; 11 and 12, eosinophile; 13, polynuclear basophile (mast cell); 14, neutrophilic myelocyte; 15, eosinophilic myelocyte; 16, mononuclear basophile (basophilic myelocyte, mast cell).

The Widal Reaction.—The agglutination of the typhoid bacillus by a typhoid serum is known as the Widal reaction. The method of obtaining this reaction is as follows: (1) To one drop of patient's serum or blood add twenty-four drops of sterile water or salt solution. (2) Make a cover-glass or hanging-drop preparation with a loopful of the dilution and another of an eighteen to twenty-four-hour culture of typhoid bacillus in bouillon. Ring the preparation with vaselin, and

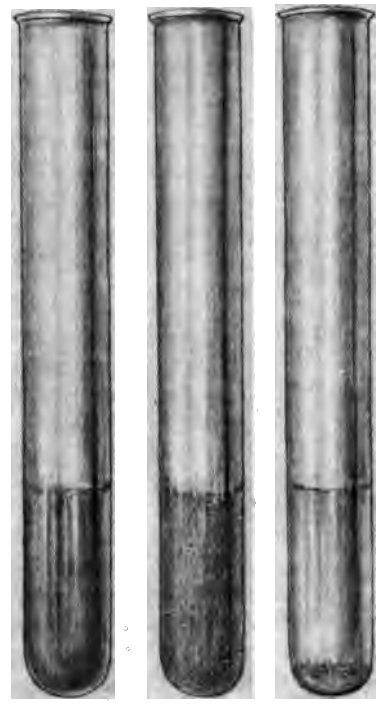


FIG. 414.—Macroscopic appearance of the Widal reaction. 1, Culture of typhoid bacillus; 2, the same culture five to fifteen minutes after the addition of immune typhoid serum; 3, the same tube after thirty minutes to one hour. Note the typhoid bacillus precipitated at the bottom of the tube leaving a clear bouillon above.

examine after fifteen, thirty, or forty-five minutes. Under the microscope the bacilli are seen to clump in irregular masses (Fig. 415). The test can also be made macroscopically, by mixing the serum and the culture in the proportions of 1–50 respectively and allowing it to stand. In time the liquid becomes flocculent, and finally the clumps settle to the bottom of the tube, leaving a clear liquid above the precipitate (Fig. 414).

Agglutination of Protozoa.—The best known agglutination in protozoa is that produced by the serum of a relapsing fever patient on *Spirocheta recurrentis*. As this organism cannot be cultivated artificially, in performing the test the blood of an infected rat should be used. Mix one loopful of the patient's serum with one loopful of defibrinated blood of a rat infected with *Spirocheta recurrentis*, and make a hanging-drop culture. Ring the preparation with vaselin and examine after from fifteen to thirty minutes. The spirochetes are seen to be agglutinated in clumps. According to Novy and others, this agglutination is so specific that it will enable one to differentiate between the four varieties of spirochetes (*i.e.*, those of African, European, Indian, and American relapsing fever). Thus, the serum of a patient that agglutinates *S. duttoni* will not agglutinate any of the

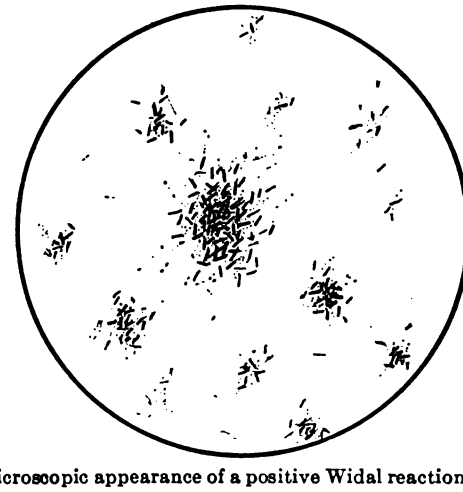


FIG. 415.—Microscopic appearance of a positive Widal reaction in typhoid fever.

other spirochetes. The test is sometimes unsatisfactory because the microörganisms perish within a short time after being exposed to the air. To avoid this, proceed as follows: (1) Mix the patient's serum and that of infected rat blood with a small portion of isotonic 2 per cent. citrate solution on the surface of a slide, and draw the mixture into a fine capillary tube. (2) Seal both ends of the tube in the flame. (3) Mount the tube on a slide with oil or balsam and apply a cover-glass. (4) Examine the preparation under the microscope. The capillary tube should be sufficiently fine so that it can be focused under the high power of the microscope.

Seroprecipitins.—Precipitins are specific substances present in the serum of an immune person. They have the power of producing a precipitate when brought in contact with the particular product or culture filtrate of the organism that causes the infection. For

example, if typhoid serum is added to a filtrate of a culture of typhoid bacillus, cloudiness appears and a precipitate is finally formed. The filtrate should be prepared from a culture of typhoid bacillus in bouillon one or two months old. This test has also been applied for the diagnosis of certain metazoan diseases, such as echinococcus infection. The method is conducted as follows: To 2 c.c. of the patient's serum (clear) add 1 to 2 c.c. of a clear filtrate of hydatid-cyst fluid. If cloudiness and a precipitate are formed, the reaction is positive.

Another test should be made with normal serum as a negative control.

The Wassermann Reaction.—The Wassermann reaction, or complement-fixation test, is now recognized as a valuable and indispensable diagnostic aid in determining the presence of syphilis. The principle of the reaction rests on the fact that the serum of syphilitic persons contains a substance (syphilitic antibodies or amboceptors) which, in the presence of an antigen (alcoholic extract of syphilitic liver, cholesterinized human heart, etc.) and a complement (normal guinea-pig serum), the complement is absorbed or combined, with the result that when a hemolytic system (antihemolytic sheep amboceptors and sheep erythrocytes) is added, no hemolysis takes place. The same test applied to non-syphilitic serum gives complete hemolysis. The reaction is specific.

Following the announcement by Wassermann of this reaction, numerous modifications appeared from time to time. Mention need be made only of those of Noguchi, Bauer, Hecht-Weinberg, Stern, and others, all based more or less upon the principle originally outlined by Wassermann. It may be said, however, that, having passed the experimental stage, the Wassermann reaction, if carefully carried out, will be found satisfactory, the particular technic employed being less important than a thorough familiarity of the serologist with the subject of hemolysis in general; the principles of the reaction, the technic of the method selected, and the reading of results. The technic outlined below is that employed by the author:

Five reagents are employed: (1) Antigen; (2) sheep erythrocytes; (3) hemolytic amboceptors; (4) complement; (5) the patient's serum.

1. *The Antigens.*—Three antigens are generally recommended for the test, namely; alcoholic extract of syphilitic liver; acetone insoluble lipoids, and cholesterinized human or ox heart.

Alcoholic Extract of Syphilitic Liver.—A fetal liver that is known to be syphilitic, and in which spirochetes are seen to be present, either by the dark-field illumination or by the Levaditi silver method of staining, is selected. (1) Add 100 c.c. of absolute ethyl alcohol to 10 grams of liver tissue finely ground with clean quartz sand. (2)

Shake the mixture mechanically for twenty-four hours or place in the incubator for from ten to twelve days, shaking it every day. The bottle should be well stoppered. (3) Filter through paper previously washed with ether and alcohol, and replace the alcohol, lost by evaporation. This is the stock extract, and is diluted 1:10 or 1:20 in salt solution for titration.

Acetone Insoluble Lipoid.—(1) Prepare extract as just directed, using normal organs, either liver or heart, and evaporate the alcohol. (2) Dissolve the residue in a sufficient quantity of ether, and allow the turbid solution to stand for a few minutes in a well-stoppered bottle. (3) Decant the ethereal extract and add a small amount of absolute alcohol—up to about one-fourth of the original volume. (4) Mix the concentrated solution with about ten parts by volume of pure acetone, and allow it to stand until the sediment settles. (5) Decant off the acetone and collect the sediment. Dry it by evaporation and weigh. (6) Dissolve the sediment in ether-alcohol, in the proportion of 1 c.c. of ether to 9 c.c. of pure ethyl alcohol for each 0.3 gram of sediment. This alcoholic solution is the stock solution from which an emulsion is prepared by mixing 1 c.c. with 9 or 19 c.c. of salt solution for titration.

Cholesterinized Alcoholic Extract.—(1) Prepare an alcoholic extract in the same way as directed for the alcoholic extract of syphilitic liver, using normal ox, guinea-pig, or the human heart, the last being preferred. (2) Add to the alcoholic extract 0.4 gram of Kahlbaum's cholesterin for each 100 c.c. (0.4 per cent.) shake, and let it stand in the ice chest over night. (3) Filter and store in tightly stoppered bottles. This is diluted 1:10 or 1:20 for titrating.

Antigens should be stored in the refrigerator, since if left at room temperature they often become inactive.

2. *The Sheep Erythrocytes.*—Sheep's blood is defibrinated and the blood-serum removed as follows: The defibrinated blood is suspended in an excess of sterile salt solution, centrifugalized, and the liquid decanted. The cells that fall to the bottom are again suspended in salt solution, centrifugalized, and the liquid again decanted. This procedure is repeated two or three times, after which the preparation is ready for use. For hemolytic work these "washed erythrocytes" are suspended in salt solution, in the proportion of 2.5 c.c. in 100 c.c. of salt solution, 1 c.c. of the suspension, equal to "one unit" of erythrocytes, being used for the test.

3. *The Hemolytic Amboceptors.*—The hemolytic amboceptors are obtained by injecting a rabbit with "washed sheep erythrocytes" free from blood-serum. These washed erythrocytes are injected into the peritoneal cavity of a rabbit. As a rule, three injections are required: The first injection consists of 2 to 5 c.c.; the second, of 5 to 10 c.c.;

and the third, of 10 to 20 c.c. of the blood. The injections are given at intervals of seven to ten days. In from ten to twelve days after the last injection the rabbit is bled and the serum separated. During the immunization not uncommonly, the animal dies of anaphylaxis after the second injection. To avoid this the author has found that a single injection of 10 to 15 c.c. of the sheep blood intraperitoneally is sufficient in most instances for the immunization of the rabbit.

A properly prepared serum should contain so much hemolytic amboceptor that about 0.1 of a 1 : 100 dilution of the serum (0.001



FIG. 416.—Rivas' apparatus for collecting blood serum. 1 and 2, the tubes disconnected; 3, both tubes in place; 4, illustration showing separation of the serum, which is collected in the lower tube, from the clot suspended by the glass invaginations in the upper tube.

mgm.) will completely hemolyze 1 c.c. of a 2.5 per cent. suspension of sheep erythrocytes, in the presence of 0.05 c.c. of normal guinea-pig serum (0.5 c.c. of a 1 : 10 dilution). When the serum is to be stored it should be mixed with equal parts of glycerin and kept in sealed ampules in the ice-chest.

There are many methods of collecting blood-serum. The bottom of a sterile test-tube may be softened in the flame, and by touching it with a piece of glass, it may be drawn into a fine cannula. For use the tip of the cannula is broken and inserted into any of the vessels

of the neck (carotid or jugular vein). The normal pressure forces the blood into the tube. The tip of the cannula is withdrawn and sealed in the flame, and the blood is allowed to coagulate. When the serum has separated, it is removed to another sterile tube with the aid of a pipet.

The blood may also be collected in a test-tube from the marginal vein of the ear, etc. In these methods, as will be seen, there is a waste of serum, since the clot and the serum remain in contact during the separation. To obviate this waste, the author some years ago devised an apparatus by which the largest amount of serum could be collected, an additional advantage being that it was absolutely free from con-

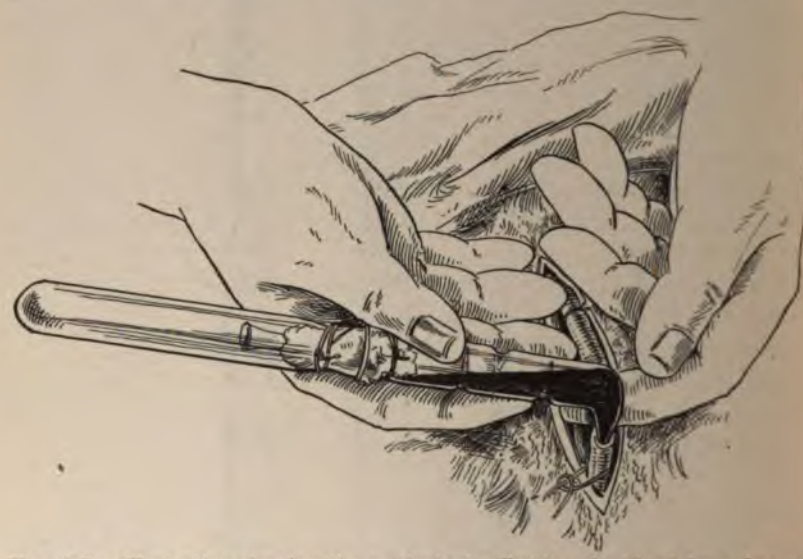


FIG. 417.—Illustration showing the method of collecting the blood from the carotid artery of a rabbit with Rivas' apparatus.

tamination. The apparatus, shown in the accompanying illustration, (Fig. 416) is easily made, consisting merely of two ordinary test-tubes constricted near the mouth and held together by a fine copper wire, cotton being placed between the tubes. The tube that is to receive the blood is provided with an invagination for holding the clot. These can easily be made by softening the glass in the flame and pushing with a pointed wooden stick toward the center. The instrument is sterilized by dry heat.

For use, make a cannula at the bottom of the tube containing the invagination by softening it in the flame, and then touching it with a piece of glass and gently drawing it out. When cool, break the tip of the cannula, insert it into an artery or vein, and collect the desired amount of blood. The blood is allowed to coagulate for from two to

four hours, after which the apparatus, with the clot on top, is placed in a test-tube rack and allowed to remain overnight. The serum is collected in the lower tube.

4. *The Complement.*—The blood of a normal guinea-pig is collected, allowed to coagulate, and the clear serum separated. There are various methods of bleeding the guinea-pig: (1) The bleeding may be made from the carotid artery: the animal being placed under ether, a flap of the skin is cut and the vessel severed. The blood is collected in a test-tube and allowed to coagulate, and the serum is collected. (2) A small incision is made through the skin in the region of the neck, the jugular vein is incised, and the blood is collected with a pipet. The wound is then sutured, and after the lapse of ten days the animal may again be bled.

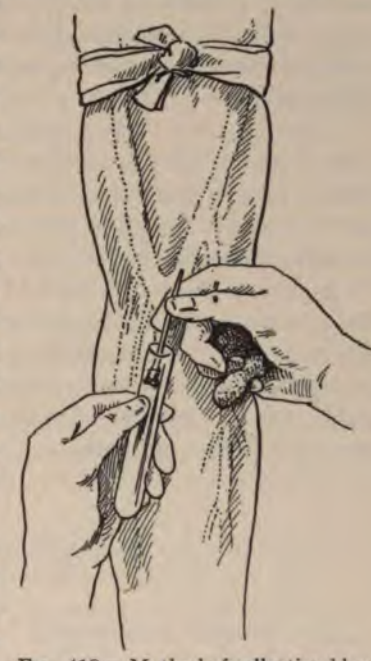


FIG. 418.—Method of collecting blood for the Wassermann reaction.

A much easier and quicker method, and one that causes no suffering on the part of the animal, consists in first rendering the guinea-pig unconscious by striking it a gentle blow on the top of the head with a hammer. A flap of skin is then cut, the carotid on one side of the neck severed with sharp scissors, and the blood collected. The entire operation should not consume more than one or two minutes.

5. *The Patient's Serum.*—This is collected from the finger or preferably from a superficial vein of the arm, when possible. A circular bandage is applied firmly above the elbow, and when the veins become prominent the point of election is sterilized by touching it with tincture of iodin. A sterile syringe needle is inserted into the vein and along its long axis. When the needle has been inserted in the proper place, the blood usually flows freely. If possible, about 5 c.c. of blood should be collected in a clean, sterile test-tube. After it has coagulated it is centrifuged and the clear serum removed with a pipet. The serum is now inactivated at 54° to 55° C. for fifteen minutes in a water-bath to destroy the complement.

The Phenomenon of Hemolysis.—Hemolysis is the liberation or escape, from the erythrocytes, of the coloring-matter of the blood—the hemoglobin. This phenomenon may take place under several con-

ditions, such as changes in the density and in the chemical composition of the blood, etc., following certain diseases. *In vitro*, if the erythrocytes are suspended in an isotonic salt solution (0.8 to 0.9 per cent.), no hemolysis occurs, but if the suspension is made in a hypotonic solution (0.2 per cent. of salt) or in tap or distilled water, hemolysis will be seen to occur very rapidly. The phenomenon also takes place if a 0.5 per cent. acetic acid solution is added to the blood. This hemolysis is not, of course, specific, since the same liquid hemolyzes the erythrocytes of any animal. If, however, a rabbit is immunized against sheep erythrocytes, the serum of the rabbit will contain *specific* hemolytic antibodies; that is, in the presence of the complement the serum of the immunized rabbit will hemolyze sheep erythrocytes only, and will exert no action upon the erythrocytes of a different species of animal.

The nature of these hemolytic antibodies is a disputed point, but they probably have a specific effect on the globin of the hemoglobin, which, by altering its chemical combination, alters or disassociates the combination and permits the escape of the coloring-matter or hematin from the erythrocytes.

An erythrocyte may be said to be made up of a plastic substance, the *hemoglobin*, and a supporting framework or *stroma*, in the meshes of which this plastic substance is contained. Furthermore, since the hemoglobin may be said to represent a combination of hematin and globin, the erythrocytes consist, therefore, of three substances, namely: stroma, hematin, and globin.

Erythrocytes { Hemoglobin { Hematin / Globin } / Stroma }

The hematin is generally believed to be the same in all blood. This is likewise true of the stroma, which merely represents the supporting framework. There remains, therefore, only the globin, which is specific, and in all probability not only varies in different species but also perhaps in different individuals of the same species.

When sheep's blood is, therefore, injected into a rabbit, the globin of the sheep erythrocytes alone is probably the substance that is concerned in the production of hemolytic antibodies. If this is the case, it would seem, therefore, that the name *sheep-erythroglobin* may properly be applied to this antigen, and that of *anti-sheep-erythroglobin* or merely *anti-erythroglobin* to the specific hemolytic anboceptors commonly known as *hemolytic sheep amboceptors*.

For the phenomenon of specific hemolysis to take place, the hemolytic amboceptor or anti-sheep-erythroglobin must be supplemented

by the presence of complement. The reaction occurs, therefore, only when the following three substances are present, namely: anti-sheep-erythroglobin or hemolytic amboceptor, sheep erythrocytes (antigen), and complement (guinea-pig serum).

Properties of the Complement.—Regarding the peculiarities of the complement, the following facts should be thoroughly understood:

1. The complement is an unstable substance. It deteriorates with time, and hence should always be used fresh (the same day).

2. It is easily destroyed or inactivated by heat at 54° to 55° C. in a few minutes.

3. Experience has shown that 0.05 c.c. (0.5 c.c. of a 1:10 dilution) of guinea-pig serum is about the amount or "*unit*" of complement required to effect complete hemolysis of 1 c.c. of a 2.5 per cent. erythrocyte suspension in the presence of at least one *unit* of hemolytic amboceptor as determined by titration.

4. Unlike ferments, the complement is exhausted or used up in the hemolytic reaction; that is, if exactly one unit of complement (0.05 c.c.) is used in the hemolytic reaction, and after complete hemolysis 1 c.c. of erythrocyte suspension and a unit of amboceptor are added to the mixture, only slight or no further hemolysis will occur.

5. Under normal conditions the strength of the complement shows only slight variation in different animals; this variation is, however, apt to be more marked in young guinea-pigs or when there is an impairment of health. It is also known that the complement may deteriorate *in vitro*, sometimes very rapidly. It is advisable, therefore, to test the potency of the complement before using it for performing the Wassermann reaction.

6. In the presence of a proper antigen, the complement has no specific affinity for uniting with hemolytic amboceptors only, but will also unite with any other variety of amboceptor (syphilitic, etc.) and be likewise exhausted, or remain combined or *fixed*, so that *if erythrocytes and hemolytic amboceptors are now added to the mixture, no hemolysis will occur*, because of the absence of, or the fixed state of the complement, as was first shown by Bordet and Gengou. It is upon this fact that the Wassermann test is based, and from it, the name *complement-fixation* test also applied to the reaction, has been derived.

7. The fresh serum of a normal adult guinea-pig should be used as complement, and while 1.5 or more units of hemolytic amboceptor and antigen, when not anticomplementary, may be used, the amount of complement should be exactly 1 unit (0.5 c.c. of 1:10 dilution of the serum). In other words, *the complement should be the standard reagent or indicator in the reaction.*

Titration of the Hemolytic Amboceptor.—Into a series of ten tubes each containing 1 c.c. of erythrocyte suspension place 0.5 c.c. of a 1:10

dilution of complement (0.05 c.c.). Now add increasing doses of inactivated immune rabbit serum (anti-sheep hemolytic amboceptors) to the tube, beginning with 0.0001 in the first tube and using 0.02 in the last tube. This is readily done by first diluting the serum 1:10 or 1:100 and using increasing quantities of the dilution. Shake the tubes and incubate at 39° to 40° C. in a water-bath for from forty-five minutes to one hour. The first tube in the series that shows complete hemolysis represents the *unit* of amboceptor. For the Wassermann test no less than about 1.5 to 2 units should be used. Two controls, one of the erythrocyte and one of the complement and erythrocytes, should be made at the same time.

TITRATION OF HEMOLYTIC AMBOCEPTORS

Tube	Inactivated Immune Serum 1:100	Complement 1:10	Erythrocytes 2.5 Per cent. Suspension	Salt Solution	Result of Hemolysis
1.....	0.01 (0.0001 undulated)	0.5 c.c.	1 c.c.	Sufficient to make 4 c.c.	No hemolysis.
2.....	0.02 (0.0002 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	No hemolysis.
3.....	0.03 (0.0003 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Beginning hemolysis.
4.....	0.04 (0.0004 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Partial hemolysis.
5.....	0.05 (0.0005 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Complete hemolysis.
6.....	0.07 (0.0007 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Complete hemolysis.
7.....	0.09 (0.0009 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Complete hemolysis.
8.....	0.10 (0.001 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Complete hemolysis.
9.....	0.15 (0.0015 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Complete hemolysis.
10.....	0.2 (0.002 undiluted)	0.5 c.c.	1 c.c.	4 c.c.	Complete hemolysis.

In this titration 0.05 c.c. of the 1:100 dilution (0.0005 c.c. undiluted serum) produced complete hemolysis. This amount is the *unit* of amboceptor, and for the Wassermann reaction 1.5 to 2 units (about 0.07 to 0.1 of the dilution) is used.

Titration of the Antigen.—(1) Prepare two series (A and B) of clean sterile test-tubes each series containing ten tubes. (2) To the first eight tubes of both series add increasing amounts of the stock antigen diluted 1:20: the first tube receives 0.05 c.c.; the second, 0.1 c.c.; the third, 0.15 c.c., etc., up to the eighth, which receives 0.4 c.c. (3) To all ten tubes of series A add 0.1 c.c. of a fresh known syphilitic serum,

inactivated, and to all ten tubes except the last of series B add 0.1 c.c. of fresh normal non-syphilitic serum, inactivated. *Neither serum, syphilitic or normal, should be anticomplementary.* (4) To all tubes of both series except the last tube of series A add 0.5 c.c. of complement diluted 1:10. Shake all tubes gently, and incubate in a water-bath for from forty-five minutes to one hour at 39° to 40° C. Shake the tubes once more during the incubation. (5) After incubation, to all the tubes of both series add the "hemolytic system." One or two units of hemolytic amboceptors and 1c.c. of 2.5 sheep erythrocytes suspension; the last tube of series B, however, receives only the erythrocytes. (6) To all tubes add salt solution to equal volume, about 4 to 5 c.c., shake, and incubate again for one hour. (7) Read the result.

The first tube of series A, containing the syphilitic serum, in which hemolysis is completely inhibited, whereas the corresponding tube of series B shows complete hemolysis, represents the *unit* of antigen, which should be used for performing the Wassermann test. A good antigen should not require more than 0.1 c.c. to 0.2 c.c. of the 1: 20 dilution to produce complete inhibition of hemolysis, and which, at the same time, in about twice that amount, does not inhibit hemolysis; in other words, *the anticomplementary dose should be about twice the size of the antigenic dose.*

The ninth tubes in both series, which have no antigen, are controls, to show any anticomplementary action of the sera; both should be completely hemolyzed. The last tube of series A, having no complement, is the patient's serum control, to show that it has been inactivated—that it is free from complement; the last tube of series B is the erythrocyte and salt control; neither tube should show any hemolysis.

It is well, too, to set a hemolytic control—a tube containing 1 c.c. of erythrocyte suspension, one unit of complement, and one or two units of hemolytic amboceptor. This should be completely hemolyzed.

Technic of the Wassermann Reaction.—In making the Wassermann test, the following precaution should be taken: (1) More than one antigen should be used; at least two, namely, alcoholic extract of syphilitic liver and cholesterinized human heart extract, and if possible a third, acetone insoluble lipoid, should be employed. (2) The test is readily performed, but requires careful manipulation and accurate measurements of all the reagents used, more especially of the complement and erythrocytes; if an error be made the test should be repeated. (3) All tubes should be properly marked, either with a number or with the initial of the patient. (4) Test-tubes, pipets, etc., should be clean and dry and, if possible, sterile. (5) The salt solution to be used for dilutions, etc., should be tested and proved to be isotonic and sterile, if possible. (6) All sera should be clear, free from erythrocytes, fresh, and, if possible, sterile. (7) Everything required for the test should

be ready and close at hand. (8) A routine method of procedure, to be followed each time, will be found most convenient, and one reagent should be used at a time. The following order is that employed by the author: Patient's serum, antigen, and complement for the first incubation and the hemolytic system; erythrocytes and hemolytic amboceptors mixed in proper proportion for the second incubation. (9) The use of wire test-tube racks will be found very convenient since they occupy little room and are easy to handle. (10) Incubation in a water-bath at 39° to 40° C. instead of in the incubator at 37° C. will be found to give more regular, constant, and uniform results.

Mode of Operation.—If, for example, five sera are to be tested proceed as follows:

1. Place four rows of test-tubes; let the front row consist of seven and place the other three in the back of eight tubes each, and mark them properly: the first tubes of each series to the left are marked plus (+) = "*syphilitic serum, positive control,*" the second are marked 0 = "*nonsyphilitic serum negative control,*" and the remaining five are marked 1, 2, 3, 4, and 5 respectively, each number corresponding to that of the patient's serum to be tested.

2. In the first four tubes on the left marked plus, place 0.1 c.c. of syphilitic serum; in the second four tubes marked 0, place 0.1 c.c. of non-syphilitic normal serum, and in the following tubes marked 1, 2, 3, 4, 5, put 0.1 c. c. of 1, 2, 3, 4, and 5 of serum, to be tested respectively. All sera should be previously inactivated.

3. To all the eight tubes of the second row, next to the front row, add one unit of syphilitic antigen, freshly diluted (0.1 to 0.2 c.c. of dilution, as determined by titration); to the next row on the back add one unit of acetone insoluble lipoid antigen, and to the last row on the back add one unit of cholesterinized antigen. It will be seen that all tubes except the front row contain antigen.

4. To all the tubes add 0.5 c.c. of complement diluted 1 : 10

5. Somewhere in the back of the rack place two tubes: one containing 1 c.c. of sheep erythrocyte suspension, 0.2 of any of the sera to be tested, inactivated, and two units of hemolytic amboceptor. This is the patient's serum complement control. The other tube receives only 1 c.c. of sheep erythrocyte suspension. This is the salt solution control, to prove that the solution is isotonic. To both tubes add enough salt solution to make about 4 c.c.

6. Titrate the amboceptor by placing it somewhere to the right or in back of five or six tubes, to which are added increasing quantities of hemolytic sheep serum diluted 1:100, beginning with 0.01 c.c. and going up to 0.2 c.c.; 0.5 c.c. of complement (1: 10 dilution) and 1 c.c. of erythrocyte suspension (2.5 per cent.), and salt solution enough to make 4 c.c.

7. Shake all tubes and incubate at 39° to 40° C. for from forty-five minutes to one hour in the water-bath, and shake the tubes once or twice more during the incubation.

8. Ascertain the unit of hemolytic amboceptor that corresponds to the first tube completely hemolyzed, and to all tubes except the two in the back to the left add the hemolytic system: 1.5 to 2 units of hemolytic amboceptor and 1 c.c. of erythrocyte suspension. Both amboceptors and erythrocytes may previously be mixed in the corresponding proportion and then added.

9. Add enough salt solution to make 4 c.c., shake the tubes, and incubate again at 39° to 40° C. for forty-five minutes. Shake once more during incubation.

The accompanying diagram (Plate XVII) shows the manner in which the tubes are arranged for making the test.

Reading of Results.—(1) Be sure that all the front tubes which are the patient's serum anticomplementary control, show complete hemolysis; also that hemolysis is complete in the last three tubes on the right of the three back rows, which are the antigen anticomplementary controls; and that the two back tubes to the left—the patient's serum complement and erythrocyte controls—are not hemolyzed.

2. See that there is no hemolysis in the back three tubes marked "plus, syphilitic serum positive control," and that all four tubes marked "0, non-syphilitic serum negative control" are completely hemolyzed.

3. The hemolytic reaction in the three back rows in the tubes marked 1, 2, 3, 4, and 5 will indicate whether the reaction is positive or negative. Thus, in *all tubes in which hemolysis is complete the reaction is* NEGATIVE, *and in all tubes in which no hemolysis has taken place or in which it is only partial the reaction is* POSITIVE.

4. It is customary to report positive reactions as plus 1, plus 2, plus 3, and plus 4. Thus plus 4 would indicate that no hemolysis has taken place when 100 per cent. inhibition; plus 3, when 75 per cent., plus 2, when 50 per cent., and plus 1, when 25 per cent. inhibition of hemolysis, as determined empirically from the amount of sediment of erythrocytes at the bottom of the tube that are unhemolyzed, as shown in Plate XVIII.

This method of reading the result of the Wassermann reaction though generally adopted, is empiric and to some extent misleading. A reaction plus 4 for instance, may be interpreted as indicating that the degree of infection of the patient is 4 units instead of plus 1 as in our general routine test we use only one unit of complement.

The method recommended by Dr. John J. Laird and used in The Department of Health of the State of Pennsylvania, which consist in substituting a plus 4 reaction by plus 1, a plus 3 by plus ¾, a plus

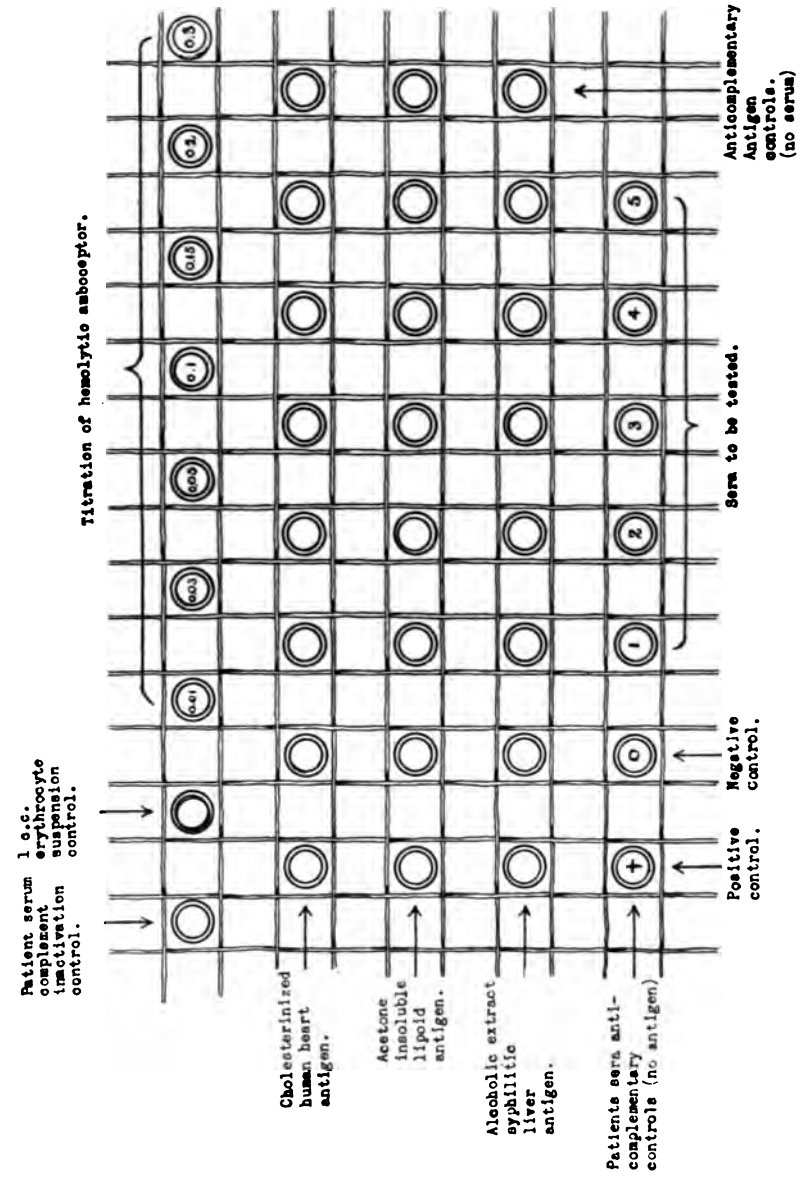


PLATE XVII.—Diagram showing the arrangement of the tubes for the Wassermann test.

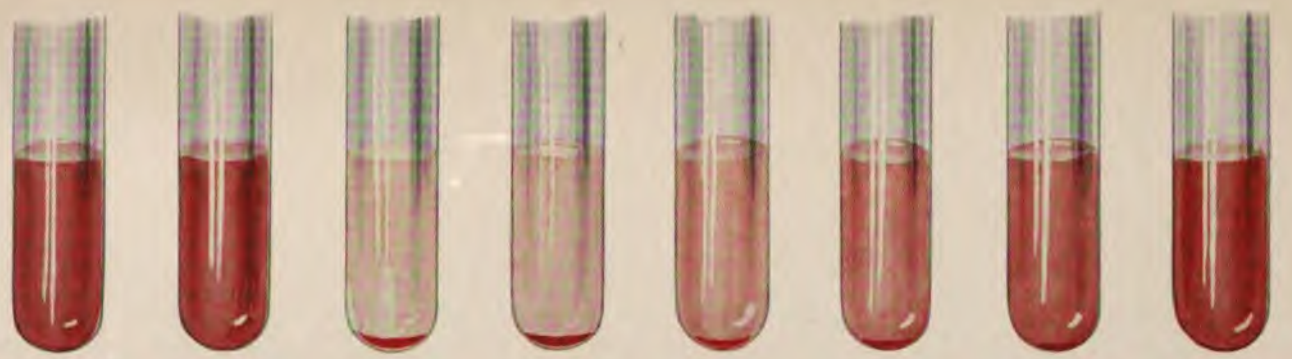


PLATE XVIII.—Showing the method of reading the results of the Wassermann test: Tube 1. Patient serum anticomplementary control, contains everything but antigen; it should be completely hemolyzed if the serum is not anticomplementary. Tube 2. Antigen anticomplementary control, contains everything but patient serum; it should be completely hemolyzed if the antigen is not anticomplementary. Tube 3. One c.c. erythrocyte suspension. Control should not show any hemolysis. Tubes 4, 5, 6 and 7 show varying degrees of a positive reaction, namely, +4 when 100 %; +3 when 75 %; +2 when 50 % and +1 when 25 % inhibition of hemolysis respectively. Tube 8. Shows a negative reaction. Hemolysis is complete.



2 by plus ½ and a plus 1 by plus ¼ is more logical and deserve due commendation as it really implys that 1, ¾, ½, and ¼, respectively, of the unit of complement used in the test has been absorbed in the reaction.

5. When the reaction is plus 4 or negative, the reading may be made from one-half to one hour after the second incubation; when, however, it is plus 1, plus 2, or plus 3, it is advisable to allow the tubes to remain in the refrigerator over night so that the erythrocytes can settle at the bottom, or the tubes may be centrifugalized from one to two hours after the second incubation, and the reading be made from the amount of sediment of erythrocytes not hemolyzed at the bottom of the tubes, as compared with the sediment in the erythrocyte control tube, which should also be centrifugalized.

6. As a rule, all antigens show the same results, but if one of them, especially one in the tubes containing the cholesterinized antigen, shows plus 1 or perhaps plus 2, whereas the other two are negative, the test is probably negative unless there is a clinical history of the case. In such cases it is advisable, when possible, to repeat the test one or two weeks later, using a fresh serum, before making a final report.

It may seem superfluous, and perhaps confusing, to use three antigens, but experience has shown the value of taking this precaution. First, it satisfies those critics who prefer one antigen to the other two; second, the technic is a simple one and consumes but little extra time; third, it serves in itself as a control; so that for this if for no other reason, if the other two antigens are not available, the three tests or at least two of them should be made with the same antigen. Finally, the use of three antigens is a source of satisfaction to the serologist, since it relieves him of any doubt when the test is negative.

The Serum Diagnosis in Metazoan Diseases.—The precipitin test has been recommended as an aid to the diagnosis of hydatid diseases. As has been stated, it consists in adding 2 c.c. of the clear hydatid liquid to 2 c.c. of the patient's serum. The appearance of cloudiness and of a precipitate in the mixture indicates a positive reaction. The same test should be performed with the serum of a normal person as control.

The complement-fixation test has also been carried out by numerous observers who use the hydatid cyst liquid previously titrated as antigen. A salt solution or alcoholic extract of a given tape-worm or nematode has also been used as antigen for making the complement-fixation test in these parasitic diseases.

These tests have been applied by many investigators (Guedini, Weinberg, Paron, Viellard, Jieni, Israel, Kolmer, etc.) in the diagnosis of hydatid cysts, Ankylostoma, Ascaris, *Tenia solum*, *T. saginata*, *Dibothriocephalus latus*, etc., and the intestinal parasites of dogs, but

the results have not been satisfactory. In the author's experience the search for the adult worm or the eggs of the parasite in the feces, urine, sputum, etc., as the case may be, is a simpler, more practical and more reliable method of diagnosis.

Bacteria in the Blood.—Years ago it was the common belief that the human tissues and blood were sterile; that is, that under normal conditions no bacteria were present in the blood. Recent investigations have, however, demonstrated that the contrary is the case. If a small amount of blood is cultured, it may not show the presence of bacteria, but if a sufficient quantity of blood is examined, bacteria will, as a rule, be found. The presence of bacteria in the blood, is due, of course, to the fact that microörganisms are constantly penetrating the mucous membrane of the intestinal tract, respiratory organs, skin, etc., and are carried into the circulation by the lymph. Under normal conditions, however, they are destroyed by the germicidal action of the tissue and blood and the normal balance is thus maintained.

Under abnormal conditions, as when the system is weakened or there is a derangement in the mucosa of the normal cavities, taking the form of ulcerations, abrasions, or wounds of the body surface, or when trauma has been inflicted on any part of the body, one of the following conditions may supervene: (1) The system may be unable to dispose of the bacteria, and as a result they may accumulate in the body; (2) gaining an entrance through abrasions, wounds, etc., and finding a favorable soil for growth, the bacteria multiply locally and eventually enter the circulation in large numbers; (3) on reaching a traumatized or otherwise diseased locality inside of the body, the bacteria may grow, set up local morbid changes, and eventually enter the circulation.

Bacteremia.—It has been seen that under any one of the abnormal conditions just described bacteria may invade the body, and, having gained an entrance, they may be either gradually destroyed or grow and multiply in the blood. It is to the latter condition, that is, *when the bacteria live, grow, and multiply in the circulating blood, that the term bacteremia should be applied.*

Bacteremia is generally understood to imply the presence of bacteria in the blood; on further thought, however, the erroneous nature of this conception become evident, since, as previously stated, and as has been demonstrated by several investigators, this is a normal and constant phenomenon.

As typical examples of bacteremic diseases anthrax and typhoid fever may be mentioned. In both of these conditions the microörganisms *B. anthracis* and *B. typhosus* respectively are found in the blood during the course of the disease, and in both the bacteria live,

grow, and multiply in the blood. Tetanus and diphtheria, on the other hand, are non-bacteremic diseases, since *B. tetanus* and *B. diphtheriæ* are not found in the blood in these conditions.

Between the two types just described there are numerous bacterial infections that are commonly pyogenic in nature; these, though originally localized affections, may eventually, under certain conditions, such as weakening of the system, etc., become generalized. A similar condition may exist when the microörganisms enter the circulation in such disproportionate numbers that the body is incapable of destroying them, with the result that the normal balance is no longer maintained and the phenomenon of infection is manifested.

Primary, Metastatic and Secondary Bacterial Infection.—By *primary bacterial infection* is understood the first lesion or infection produced by the entrance of pathogenic bacteria into the body. As examples of primary infection diphtheria, typhoid fever, tetanus, and anthrax may be mentioned.

Metastatic Bacterial Infection.—A metastatic bacterial infection is one in which the bacteria are disseminated, either through the blood or lymph, from the primary focus of infection to different parts of the body. Focal abscesses of the liver following suppuration in another part of the body; miliary tuberculosis, which normally is always secondary to tuberculosis in other organs, etc., are examples of metastatic infections.

Secondary Infection.—A secondary infection is a non-metastatic bacterial infection that is different in nature from the original disease. Abscesses of the lung following tuberculosis and paragonimiasis are examples of secondary infections. A secondary infection, therefore, presupposes a predisposing condition that favors the growth and multiplication of pathogenic bacteria in any part of the body, and in this sense it may be said that most, if not all, primary infections are secondary in nature, since a weakening of the system or a previous pathologic condition of the part is necessary for growth and multiplication of pathogenic bacteria to take place. Thus, an abrasion or a wound in the skin is essential for the entrance and growth of anthrax and tetanus bacillus in the body; a sore throat and bronchitis, when accompanied by vascular disturbances in the lung, are the primary lesions that predispose to the development of pneumonia.

A secondary infection may in turn become metastatic. Thus, an abscess of the lung following paragonimiasis may give rise to focal abscesses in any part of the body.

Secondary Bacterial Infection in Parasitic Diseases.—Most of the parasitic diseases of man could properly be considered as offering no immediate danger to the patient were it not for the fact that they constantly predispose the patient to secondary bacterial infections

that are not uncommonly the cause of death. This is well illustrated, as already stated, in the case of paragonimiasis of the lungs. Here the presence of the paragonimus gives rise merely to a localized area of consolidation (Plate III), but predisposes the patient to the development of abscesses of the lung (Fig. 7), which in turn may give rise to metastatic lesions or to a generalized bacteremia. This is also true of cases of tuberculosis, uncinariasis, dysentery, and ulcerations of the intestines which predispose the patient to a generalized bacterial infection.

Blood Culturing.—In making blood cultures the blood should be collected, under strict aseptic precautions, from any of the superficial



FIG. 419.—Method of collecting blood for blood cultures.

veins of the arms. The area selected should be washed with warm water and soap, followed by alcohol, and then touched with tincture of iodin (10 per cent. in 80 per cent. alcohol). From 5 to 10 c.c. of blood are collected in a sterile test-tube containing glass beads; the blood is defibrinated by shaking it for five to ten minutes, the cotton plug being replaced during defibrination (Fig. 419). The defibrinated blood is now cultured in bouillon, blood agar, coagulated blood-serum, serum bouillon, etc., incubated at 37° C. for from twenty-four to forty-eight hours or longer, and examined for the presence of bacteria. The following bacteria may be found in the blood: *Bacillus typhosus; B.*

paratyphosus; B. coli; B. anthracis; B. pestis; B. tuberculosis during the early stage of acute miliary tuberculosis; *B. leprœ, B. diphtheriæ,* in very grave and marked infection; *B. pyocyaneus; B. diphtheroides; B. pneumoniæ,* and the pyogenic cocci.

Mycosis.—Fungoid diseases are generally localized; the parasite of *thrush,* however, and possibly a few other fungi, are occasionally found in the blood in the form of yeast-like bodies in cases of blastomycosis.

Protozoan Parasites.—The following protozoan parasites may be found in the blood: The plasmodia of malaria; *Trypanosoma gambiense* and *T. cruzi; Babesia hominis(?);* the microörganism of kala-azar; the spirochetæ of relapsing fevers, and occasionally *Treponema pallidum.*

Metazoan Parasites.—The most important of all metazoan parasites of the blood are the Filaria, whose embryos, or microfilariæ, are found in the circulation. The most important are the microfilariæ of *Filaria bancrofti, F. loa, F. perstans,* and *F. demarquayi.* In addition, the adult parasite and egg of Schistosoma, the egg of Paragonimus, and the larvæ of Ankylostoma, Strongyloides, and Trichinella may, in rare instances, be found in the blood.

The Cerebrospinal Fluid.—The cerebrospinal fluid is a clear liquid, alkaline in reaction, and having a specific gravity of 1005–1010. It contains small quantities of glucose, which reduces Fehling's solution, and proteid substances (globulin). The normal fluid is not coagulated by heat, but a slight precipitate may be formed when dilute acetic acid solution is added before boiling.

Normally the cerebrospinal fluid is almost free from cellular elements, since it does not contain more than 10 cells to the cubic millimeter (2–4 cells to the field). These cells are chiefly lymphocytes, but a few endothelial cells may be found. In certain morbid conditions, such as tumors, syphilis, tuberculosis, pyogenic infections of the brain, and in parasyphilitic diseases, such as tabes and paresis, the globulin content and cellular elements in the liquid are increased, the lymphocytes or polynuclear leukocytes predominating, as the case may be.

Technic of Lumbar Puncture.—The patient may be seated either in bed or in a chair, with the body inclined forward, or he may be placed on the side on the edge of the bed, with the head slightly elevated. In most cases especially in children and sick persons, the latter position is preferable (Fig. 420).

A needle about 8 to 10 cm. long and having a bore of 1 to 1.5 mm., well pointed, with cutting edges at the tip, and made of a flexible, non-rigid material, such as platinum or gold, should be used for the operation. Select a soft spot between the third and fourth lumbar spinous processes, corresponding to about the level of the crest of the

ilium. Wash the part with soap and water, followed by alcohol, and touch it with tincture of iodin. The needle is grasped firmly, and with a sudden thrust it is inserted in the median line through the skin and muscle down to the spinous ligaments. It is now pushed on more slowly until the canal is reached, which is manifested by a sudden sensation of "giving way." If desired, the lateral route can be used instead of the median line.

The first fluid that appears is usually stained with blood and should be collected in a separate tube. From 5 to 10 c.c. of fluid free from blood should be collected in another tube, the needle removed, the part touched with tincture of iodin, and collodion applied.



FIG. 420.—Technic of spinal puncture.

If no fluid appears, the needle may be inserted a little further, if it has not entered the canal, or withdrawn a trifle, and if, after this, the tap proves a dry one, it is not advisable to make another puncture.

Determination of Total Number of Cells.—Under normal conditions of when the spinal fluid is rich in cells, it may be examined directly by the same method used in counting the blood-cells with the hemocytometer, except that the serum used is not diluted. Or as a routine procedure a given quantity of the serum is centrifuged, the liquid decanted whether sediment is present or not, the volume of the residue measured, and the cells counted. The total number of cells in 1 c.mm. of the liquid is determined by calculation. Thus, if the residue, after centrifugalization of 5 c.c. of the liquid, is 0.5 c.c., and this shows 5000 cells per c.mm., the total number will be 500 per c.mm. (5000 ÷ 10).

Differential Count.—The differential count is made in the same manner as it is done for the blood. Spread preparations of the sedi-

ment are made and stained by hematoxylin-eosin, methylene-blue, or Wright's stain.

The Cerebrospinal Fluid for Making the Wassermann Test.—Instead of serum, the cerebrospinal fluid may be used for making the Wassermann test, from 0.5 to 1 c.c. being used.

Noguchi's Butyric-acid Test.—Into a small, thin-walled test-tube place 0.2 c.c. of cerebrospinal fluid that is clear and free from blood. Add 1 c.c. of a 10 per cent. solution of butyric acid in normal salt solution, and boil for a short time over a low flame. Next add 0.2 c.c of a normal solution of sodium hydroxid and boil again for a few seconds. An increase of protein content (globulin) in the liquid is indicated by the appearance of a granular or flocculent precipitate, which gradually settles to the bottom of the tube, leaving a clear liquid above it.

The speed with which the reaction occurs varies with the amount of protein present. It may appear in a few minutes or in one or two

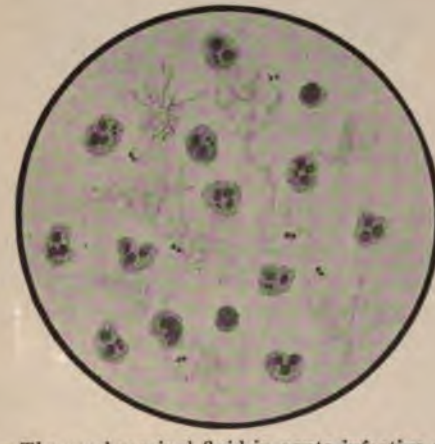


FIG. 421.—The cerebrospinal fluid in acute infective meningitis.

hours, which is the time limited for the test. *A slight opalescence of the liquid, without the formation of a distinct precipitate, may be regarded as normal.*

The Cerebrospinal Fluid in Sleeping Sickness.—Castellani demonstrated the presence of *Trypanosoma gambiense* in the cerebrospinal fluid. For the detection of this flagellate the fluid is centrifugalized and the sediment examined either in the fresh state or after staining it with Giemsa's, methylene-blue, or other stains.

Interpretation of Results.—(1) In all inflammatory or irritating conditions of the brain and spinal cord the globulin and cell content are usually increased.

2. In the acute stage of simple suppurative meningitis, the poly-

nuclear leukocytes are abundant (Fig. 421), but later, in the chronic stage, the lymphocytes may predominate.

3. In tuberculous meningitis, especially in the early stage, the lymphocytes are abundant, but later in the course of the disease, when secondary infection and suppuration are prone to occur, the polynuclear cells predominate.

4. The presence of erythrocytes is suggestive of hemorrhage or fault in technique.

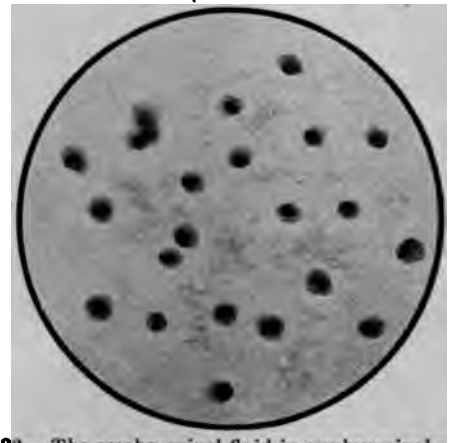


FIG. 422.—The cerebrospinal fluid in cerebrospinal syphilis.

5. An increase of globulin and lymphocytes with a negative Wassermann is suggestive of meningeal tuberculosis, disseminated sclerosis, syringomyelia, tabes dorsalis (non-syphilitic), leprosy of the central nervous system, or some chronic inflammation, whereas a positive Wassermann, of course, indicates syphilis.

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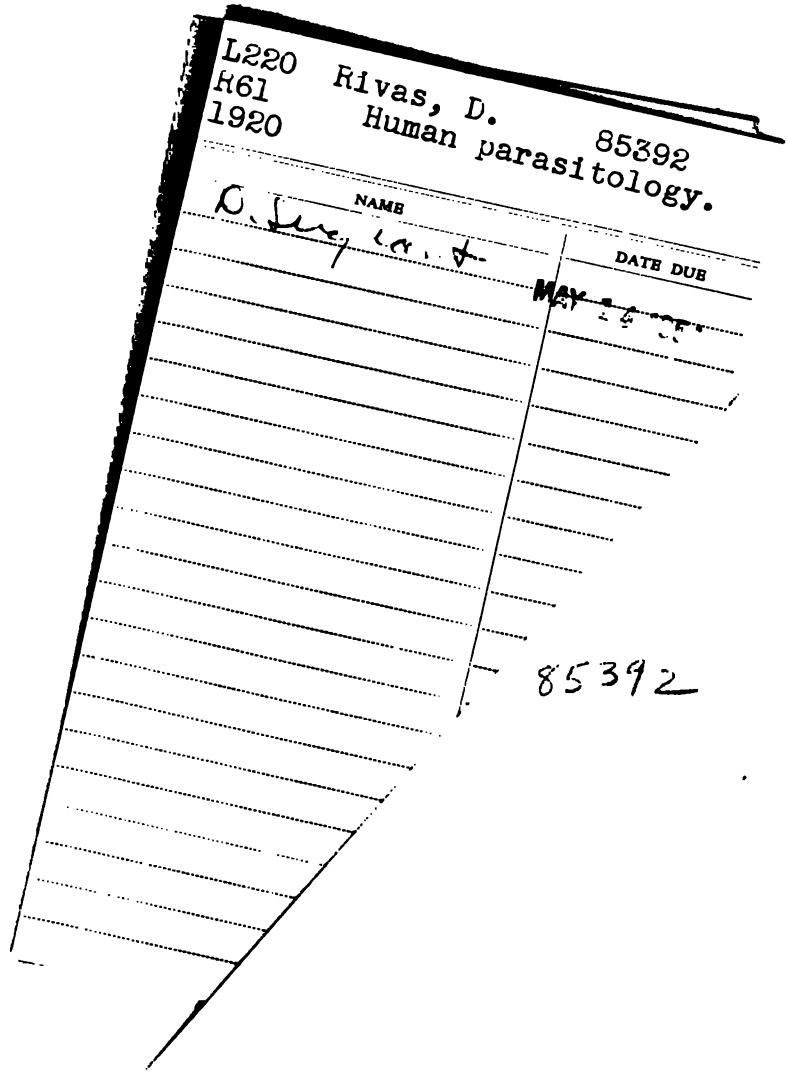
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